Mallari, Patricia

From: Horrigan, Jeanne (ASRC)
Sent: Thursday, November 10, 2005 11:03 AM
To: Mallari, Patricia
Subject: Search Results for Serial 10/089835

Hi Tricia,

Attached are the search results for the correlation between cyanide/isopropanl in the breath and the presence of liver disease. I underlined the titles of the references that I thought were most relevant, but I suggest that you review ALL the results.

LiverallF.rtf

I hope this is helpful. Please let me know if you have any questions or would like additional searching on this application.

Best regards,
Jeanne Horrigan
ASRC Searcher
EIC3700
RND 8B31
Phone 23529

STIC Search Report
EIC 3700

STIC Database Tracking Number: 169478

TO: Patricia Mallari
Location: RND 7b31
Art Unit: 3736

Pinhole Cameras 10/089835

From: Jeanne Horrigan
Location: RND 8A34
Phone: 571-272-3529

jeanne.horrigan@uspto.gov

Search Notes

Attached is your copy of your search request for the cyanide/isopronol and liver disease connection. I sent you the results of the search by email earlier this morning.

Also attached is a search feedback form. Completion of the form is voluntary. Your completing this form would help us improve our search services.

I hope the attached information is useful. Please feel free to contact me if you have any questions or need additional articles on this subject.

JH

169478

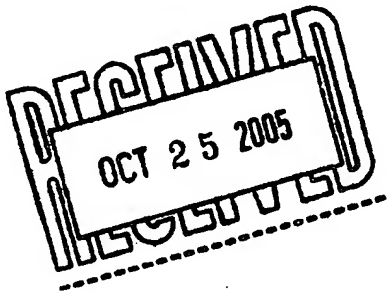
For Jeanne

Solomon, Terrance

From: Mallari, Patricia
Sent: Tuesday, October 25, 2005 12:14 PM
To: STIC-EIC3700
Subject: Database Search Request

A redo of a previous search request.

Requester:
Patricia Mallari (TC3700)
Art Unit:
3736
Employee Number:
78576
Office Location:
RND 7B31
Phone_Number:
(571) 272-4729
Mailbox Number:



Case serial number:
10/089835
Class / Subclass(es):
600/532
Earliest Priority Filing Date:
10/6/00
Format preferred for results:
E-mail
Search Topic Information:
A correlation between cyanide or isopropanol in the breath and the presence of hepatic (liver) disease.

synonyms for isopropanol include 2-propanol and isopropyl alcohol.
Special Instructions and Other Comments:
The best times to contact me are weekdays between 1:30 pm and 6 pm.

I'm requesting that Jeanne Horrigan do this search.

Isopropanol RN = 67-63-0

Cyanide RN =

NON-PATENT LITERATURE

```
File 155:MEDLINE(R) 1951-2005/Nov 08
         (c) format only 2005 Dialog
File 156:ToxFile 1965-2005/Nov W1
         (c) format only 2005 Dialog
File 159:Cancerlit 1975-2002/Oct
         (c) format only 2002 Dialog
File   5:Biosis Previews(R) 1969-2005/Nov W1
         (c) 2005 BIOSIS
File  73:EMBASE 1974-2005/Nov 10
         (c) 2005 Elsevier Science B.V.
File 317:Chemical Safety NewsBase 1981-2005/Nov
         (c) 2005 Royal Soc Chemistry
File  50:CAB Abstracts 1972-2005/Oct
         (c) 2005 CAB International
File  74:Int.Pharm.Abs 1970-2005/Oct B2
         (c) 2005 The Thomson Corporation
File 376:Derwent Drug File 1964-1982
         (c) 1995 Thomson Derwent
File 377:Derwent Drug File 1983-2005/Oct W5
         (c) 2005 Thomson Derwent.
File 162:Global Health 1983-2005/Oct
         (c) 2005 CAB International
File   6:NTIS 1964-2005/Oct W5
         (c) 2005 NTIS, Intl Cpyrght All Rights Res
File 319:Chem Bus NewsBase 1984-2005/Nov 10
         (c) 2005 Elsevier Eng. Info. Inc.
File  94:JICST-EPlus 1985-2005/Sep W1
         (c)2005 Japan Science and Tech Corp(JST)
File  99:Wilson Appl. Sci & Tech Abs 1983-2005/Oct
         (c) 2005 The HW Wilson Co.
File  35:Dissertation Abs Online 1861-2005/Oct
         (c) 2005 ProQuest Info&Learning
File  65:Inside Conferences 1993-2005/Nov W1
         (c) 2005 BLDSC all rts. reserv.
File 431:MediConf: Medical Con. & Events 1998-2004/Oct B2
         (c) 2004 Dr. R. Steck
Set     Items   Description
S1      20338   RN=57-12-5 OR RN=67-63-0
S2     296632   CYANIDE OR CARBON()NITRIDE()ION OR HYDROCYANIC()ACID OR IS-
              OCYANIDE OR NITRILE()ANION OR CN OR CN1
S3      36273   (ISOPROPYL OR ISO()PROPYL OR SEC()PROPYL)()ALCOHOL OR (ISO
              OR 2)()PROPANOL OR ISOPROPANOL OR DIMETHYLCARBINOL OR IPA
S4     658269   HEPATITIS OR CIRRHOSIS OR RIFT()VALLEY()FEVER
S5     222210   CHIARI? ?()SYNDROME OR HEPATIC()VEIN()THROMBOSIS OR HEPATO-
              CELLULAR(N)CARCINOMA? ? OR HEPATOMA OR PORTOSYSTEMIC()ENCEPHA-
              LOPATHY
S6    1071768   HEPATIC OR LIVER(1N)(DISEASE? ? OR NECROSIS OR TUMOR? ? OR
              TUMOUR? ? OR CANCER? ? OR NEOPLASM? ?) OR HEPATOTOXICITY
S7    2390690   LIVER
S8     200347   BREATH OR EXHALATION OR EXPIRATORY OR EXHALE? ? OR EXHALING
S9      20768   EXPIRATION
S10    333122   S1:S3
S11      8537   S10 AND S4:S6
S12     16199   S10 AND S7
S13        26   S8 AND S11
```

S14	49	S8 AND S12
S15	7	S9 AND S11
S16	4	S9 AND S12
S17	65	S13:S16
S18	49	RD (unique items)
S19	4	S18/2001:2002
S20	3	S18/2003:2004
S21	3	S18/2005
S22	39	S18 NOT S19:S21
S23	**39**	**Sort S22/ALL/PY,A**

S1 1 CYANIDE/TI AND BREATH/TI

1/9/1
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2005 Dialog. All rts. reserv.
08275589 PMID: 2837167
The origin of hydrogen cyanide in breath.
Lundquist P; Rosling H; Sorbo B
Department of Clinical Chemistry, Linkoping University, Uppsala, Sweden.
Archives of toxicology (GERMANY, WEST) 1988, 61 (4) p270-4, ISSN 0340-5761 Journal Code: 0417615
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

The excretion of hydrogen cyanide in breath and blood concentrations of cyanide were measured in eight normal subjects. There was no correlation between breath and blood levels of cyanide. Furthermore, breath cyanide concentrations calculated from blood values were much lower than measured values, which suggested a local production of hydrogen cyanide in the oropharynx. When saliva was incubated at 37 degrees C hydrogen cyanide was formed in the presence of air but not in a nitrogen atmosphere. No hydrogen cyanide was formed with boiled saliva and the production of hydrogen cyanide by native saliva was inhibited by catalase and by 6-n-propyl-thiouracil. Centrifugation of saliva resulted in a supernatant and a sediment, which were both required for the formation of hydrogen cyanide. Dialysis of the supernatant abolished its cyanide forming ability, which could be restored by addition of thiocyanate. We conclude that most of the hydrogen cyanide found in breath from normal human beings originates from oxidation of thiocyanate by salivary peroxidase in the oropharynx. As a consequence measurements of breath hydrogen cyanide can only be used to detect heavy exposure to cyanide.

Record Date Created: 19880624
Record Date Completed: 19880624
Tags: Female; Male; Research Support, Non-U.S. Gov't
Descriptors: *Breath Tests; *Hydrogen Cyanide--metabolism--ME; Adult; Humans; Hydrogen Cyanide--blood--BL; Hydrogen-Ion Concentration; Methemoglobin--metabolism--ME; Saliva--metabolism--ME; Salivation; Thiocyanates--metabolism--ME
CAS Registry No.: 0 (Thiocyanates); 74-90-8 (Hydrogen Cyanide); 9008-37-1 (Methemoglobin)

23/6/1 (Item 1 from file: 156)
350469 NLM Doc No: NIOSH/00141624 Sec. Source ID: NIOSH/00141624

Acetonecyanhydrin Poisoning In Man And Animals; Experimental Research On Percutaneous Toxicity Of Acetoanhydrin
1955

23/6/4 (Item 4 from file: 156)
374764 NLM Doc No: NIOSH/00173411 Sec. Source ID: NIOSH/00173411
Acrylonitrile: In Vivo Metabolism in Rats and Mice
1981

23/6/5 (Item 5 from file: 155)
06464176 PMID: 7141555
Metabolism of 1-propyl-1-nitrosourea (PNU) in rats.
1982

23/6/6 (Item 6 from file: 155)
06444645 PMID: 7132572
Isopropanol **enhancement of carbon tetrachloride metabolism in vivo.**
Aug 16 1982

23/6/7 (Item 7 from file: 73)
02433454 EMBASE No: 1983144465
Comparative metabolism of 2-nitropropane in rats and chimpanzees
1983

23/6/8 (Item 8 from file: 73)
02380151 EMBASE No: 1983149162
Comparative toxicokinetics of 2,3-sup 1sup 4C- and 1-sup 1sup 4C-acrylonitrile in the rat
1983

23/6/9 (Item 9 from file: 377)
00136415 DERWENT ACCESSION NUMBER: 85-36086
Forensic Science., 1985

23/6/14 (Item 14 from file: 155)
08407165 PMID: 3142098
Disposition of inhaled 1-chloro- 2 - propanol **in F344/N rats.**
Sep 30 1988

23/6/15 (Item 15 from file: 156)
417715 NLM Doc No: NIOSH/00191442 Sec. Source ID: NIOSH/00191442
Lipid Peroxidation in Acrylonitrile-Treated Rats, Evidenced by Elevated Ethane Production
1989

23/6/16 (Item 16 from file: 94)
01192002 JICST ACCESSION NUMBER: 91A0165307 FILE SEGMENT: JICST-E
Studies on the metabolic fate of (.+-.)-1-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)-3-isopropylamino- 2 - propanol **hydrochloride (betaxolol hydrochloride) (1): Absorption, distribution, metabolism and excretion after single administration to rats.**, 1990

23/6/17 (Item 17 from file: 155)
09110439 PMID: 2400471
Bioavailability of iron and cyanide **from 59Fe- and 14C-labelled hexacyanoferrates(II) in rats.**

Jun 1990

23/6/19 (Item 19 from file: 73)
05127173 EMBASE No: 1992267389
Variable severity of pulmonary disease in adults with identical cystic fibrosis mutations
1992

23/6/21 (Item 21 from file: 155)
10039367 PMID: 1479773
[Isolated congenital tricuspid valve insufficiency--case report]
Izolowana, wrodzona niedomykalnosc zastawki trojdzielnej--opis przypadku.
Sep 1992

23/6/22 (Item 22 from file: 155)
09949611 PMID: 1414450
Alpha 1-antitrypsin-deficiency-related emphysema.
Sep-Oct 1992

23/6/26 (Item 26 from file: 73)
06717443 EMBASE No: 1996211281
Pulmonary function in children with homozygous·alphainf 1-protease **inhibitor deficiency**
1996

23/6/28 (Item 28 from file: 73)
06591152 EMBASE No: 1996255811
Respiratory insufficiency at birth: A predictor of mortality for infants with omphalocele
1996

23/6/34 (Item 34 from file: 73)
11048102 EMBASE No: 2000393129
Congenital Listeria monocytogenes sepsis
2000

23/6/36 (Item 36 from file: 73)
10873473 EMBASE No: 2000357303
Outcome of gastrointestinal complications after liver **transplantation for familial amyloidotic polyneuropathy**
2000

23/6/39 (Item 39 from file: 156)
923340 NLM Doc No: RISKLINE/6050010 Sec. Source ID: RISKLINE/KemI UI:1996050010
2-Ethylhexanol

23/9/10 (Item 10 from file: 94)
DIALOG(R)File 94:JICST-EPlus

00066385 JICST ACCESSION NUMBER: 85A0189455 FILE SEGMENT: JICST-E
Studies on isopropanol **metabolism and poisoning.**
IDOTA SACHIKO (1)
(1) Nihon Univ., School of Medicine
Nichidai Igaku Zasshi(Journal of Nihon University Medical Association), 1985, VOL.44,NO.1, PAGE.39-47, FIG.12, TBL.3, REF.20

JOURNAL NUMBER: F0911AAO ISSN NO: 0029-0424 CODEN: NICHA
UNIVERSAL DECIMAL CLASSIFICATION: 615.917 616.39-099
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication
DESCRIPTORS: rat; drug poisoning; alcohol dehydrogenase; tissue concentration; human(primates); **liver** ; blood concentration; starvation; **expiratory** excretion; diabetes mellitus; oral administration; aliphatic alcohol; aliphatic ketone; deoxysugar; nitrogen heterocyclic compound
BROADER DESCRIPTORS: Myomorpha; Rodentia; Mammalia; Vertebrata; animal; poisoning(disease); disease; alcohol oxidoreductase; oxidoreductase; enzyme; concentration(ratio); degree; bile duct system; digestive organ ; malnutrition; nutrition disorder; disorder/trouble/obstacle; metabolic disease; excretion; administration route; administration(biology); alcohol; hydroxy compound; ketone; carbonyl compound; carbohydrate; heterocyclic compound
CLASSIFICATION CODE(S): GZ02030Y; GD06010Q

23/9/13 (Item 13 from file: 377)
DIALOG(R)File 377:Derwent Drug File

00289976 DERWENT ACCESSION NUMBER: 88-34781
Enhanced In Vivo-Lipid Peroxidation Associated with Halothane Hepatotoxicity **in Rats.**
Younes M; Heger B; Wilhelm K P; Siegers C P
Pharmacol.Toxicol. 63, No. 1, 52-56, 1988
CODEN: 7404R ISSN: 0901-9928 LANGUAGE: English RECORD TYPE: Abstract
REPRINT ADDRESS: Institute of Toxicology, School of Medicine, University of Luebeck, Ratzeburger Allee 160, D-2400 Luebeck, West Germany.
ABSTRACT:
Exhaled ethane (EN) levels were normal in non- or phenobarbital(PB)-induced rats exposed to halothane (HA) under normoxic conditions. Under hypoxic conditions, PB-induced rats and GSH-depleted rats had increased EN **exhalation** on exposure to HA and serum GPT and sorbitol dehydrogenase (SDH) activities were increased. GSH was depleted by i.p. phorone injection. Pretreatment with i.v. deferroxamine (DF), diethyldithiocarbamate p.o. (DE) or p.o. catechin (**CN**) of GSH-depleted. PB-induced rats exposed to HA under hypoxic conditions, suppressed EN **exhalation** ; only **CN** suppressed the increase in SDH activity. The level of thiobarbituric(TA)-reactive material was doubled; DF, DE or **CN** suppressed the effect. HA-induced **liver** damage may be associated with increased rates of lipid peroxidation.
SPECIAL FEATURES: 2 Fig. 4 Tab. 23 Ref.
LINK TERMS:
01; HALOTHANE --DM; HALOTHANE --AE; HEPATOPATHY --AE; PHENOBARBITAL --RC; GLUTATHIONE --RC; PHORONE --RC; DEFEROXAMINE --RC; DIETHYLDITHIOCARBAMATE --RC; CIANIDANOL --RC; TOX. --FT; BLOOD-SERUM --FT ; CONC. --FT; EC-2.6.1.2 --FT; EC-1.1.1.14 --FT; HYPOXIC --FT; IN-VIVO --FT; RAT --FT; LIVER --FT; LIPID-PEROXIDATION --FT; HYPOXIA --FT ; OXYGEN --FT; ALANINE-AMINOTRANSFERASE --FT; L-IDITOL-DEHYDROGENASE --FT ; LAB.ANIMAL --FT; LIPID-METAB. --FT; GEN.ANESTHETICS --FT; HALOTHANE --RN; DM --FT; AE --FT
SECTION HEADINGS: Endogenous Compounds (22); Toxicology (34); Anesthetics(45)
THEMATIC GROUPS: P (Pharmacology); B (Biochemistry); S (Adverse Effects)

23/9/20 (Item 20 from file: 73)
DIALOG(R)File 73:EMBASE

05014438 EMBASE No: 1992154654
Characteristics of a new urine, serum, and saliva alcohol reagent strip
Tu G.-C.; Kapur B.; Israel Y.
Primary Mechanisms Research, Addiction Research Foundation, 33 Russell Street,Toronto, Ont. M5S 2S1 Canada
Alcoholism: Clinical and Experimental Research (ALCOHOL. CLIN. EXP. RES.) (United States) 1992, 16/2 (222-227)
CODEN: ACRSD ISSN: 0145-6008
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
We have tested an ethanol reagent strip developed at the Addiction Research Foundation of Ontario. Alcohol dehydrogenase and nicotinamide adenine dinucleotide, in the presence of pyrazole, react with ethanol to yield acetaldehyde plus reduced nicotinamide adenine dinucleotide. The latter reduces iodonitrotetrazolium chloride in the presence of diaphorase, generating an intense red color. The rate of color development is proportional to the concentration of ethanol. Color is compared at a specific time against a calibrated color scale ranging from green (negative) to red, representing alcohol concentrations of 0, 25, 50, 100, 200, and 400 mg/dl (0- 0.4%; 0-87 mmol/liter). We were able to interpolate the color observed between the calibrated blocks. When tested on urine, serum/plasma, and saliva, ethanol concentration determined by the reagent strip correlates well with ethanol concentration as determined by gas chromatography or by automated enzymatic analysis ($r = 0.92-0.98$, $p < 0.001$; slope 0.83-1.16). The reagent strip was shown to be used appropriately by nonexperienced individuals following a 1-min explanation (reagent strip values, $r = 0.92$; $p < 0.001$, slope = 0.97, versus gas chromatography). **The reagent strip does not react with methanol (wood alcohol), isopropanol (rubbing alcohol)**, and ethylene glycol (antifreeze) often found in accidental poisonings. In 379 clinical samples obtained without exclusion criteria from 12 hospital emergency rooms and a **liver** clinic, the sensitivity of the reagent strip in detecting ethanol was 98%.
Specificity was 99%. The reagent strip was found to have virtually unlimited stability under refrigeration (4degreeC) and to be stable for 3 to 4 months at room temperature (22-23degreeC). The reagent strip should be valuable in a number of clinical settings in which rapid assessment of alcohol intoxication or of alcohol consumption, using either of the biological fluids (urine/serum/saliva), is wanted and in which a specific and sensitive method to determine alcohol requiring no instrumentation is needed.
DRUG DESCRIPTORS:
*acetaldehyde; *alcohol; *alcohol dehydrogenase; *nicotinamide adenine dinucleotide; *pyrazole
MEDICAL DESCRIPTORS:
*alcohol blood level; *diagnostic test; *saliva analysis; *urine level accuracy; alcohol intoxication--diagnosis--di; article; **breath** analysis; diagnostic accuracy; gas chromatography; human; priority journal; standard
CAS REGISTRY NO.: 75-07-0 (acetaldehyde); 64-17-5 (alcohol); 9031-72-5 (alcohol dehydrogenase); 53-84-9 (nicotinamide adenine dinucleotide); 288-13-1 (pyrazole)
SECTION HEADINGS:
040 Drug Dependence, Alcohol Abuse and Alcoholism

23/9/37 (Item 37 from file: 156)
DIALOG(R)File 156:ToxFile

735657 NLM Doc No: CRISP/2000/ES80055-04 Sec. Source ID: CRISP/2000/ES80055-04

COMPARATIVE METABOLISM AND MECHANISMS OF TOXICITY OF NTP CHEMICALS

GHANAYEM BI
NIEHS, NIH

Source: Crisp Data Base National Institutes of Health
Pub. Year: 2000
Sponsoring Agency: U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INSTITUTES OF HEALTH, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
Award Type: Intramural Project
Document type: Research
Languages: ENGLISH
Record type: Completed
Subfile: CRISP

Gavage administration of MAN to rats causes olfactory epithelial metaplasia and necrosis. In rats, MAN is metabolized to acetone which is eliminated along with parent MAN in **breath** . Since acetone is a known inducer of CYP2E1, we hypothesized that acetone **exhalation** may result in increased expression of CYP2E1 in the olfactory tissue leading to increased in situ formation of cytotoxic MAN metabolites. To address this hypothesis, male F344 rats received 60 mg MAN /kg and were sacrificed 6, 12, or 24 hr after a single dose, or 24 hr after 7 consecutive da ily doses. RT-PCR, Western blotting, and immunohistochemical staining were used to determine CYP2E1 expression, and chlorzoxazone hydroxylation was used to assess CYP2E1 catalytic activity. Present results showed that CYP2E1 mRNA was increased in lung and olfactory tissues with minimal effect in the **liver**. Further, CY P2E1 protein expression increased in lung, olfactory, and **liver** tissues. These data showed that administration of MAN to rats causes increased expression of CYP 2E1 in lung and olfactory. These results also showed that acetone, similar to MAN, induces the expression of CYP2E1 at both the transcriptional and post-transcriptional levels in rat nasal and lung tissues. Further, under the conditions used in this work, increased expression of CYP2E1 in the **liver** of MAN-treated rats is apparently limited to post-transcriptional mechanisms.

Identifiers: laboratory mouse; urinalysis; **cyanide** ; **breath test** ; drug metabolism; cytochrome P450; **liver** metabolism; biotransformation; toxicology; enzyme activity
Record Date Created: 200108

```
File  34:SciSearch(R) Cited Ref Sci 1990-2005/Oct W5
         (c) 2005 Inst for Sci Info
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
File 144:Pascal 1973-2005/Oct W5
         (c) 2005 INIST/CNRS
File  91:MANTIS(TM) 1880-2005/Jun
         2001 (c) Action Potential
File 164:Allied & Complementary Medicine 1984-2005/Nov
          (c) 2005 BLHCIS
File 467:ExtraMED(tm) 2000/Dec
         (c) 2001 Informania Ltd.
Set     Items   Description
S1      74815   CYANIDE OR CARBON()NITRIDE()ION OR HYDROCYANIC()ACID OR IS-
             OCYANIDE OR NITRILE()ANION OR CN OR CN1
S2      21190   (ISOPROPYL OR ISO()PROPYL OR SEC()PROPYL)()ALCOHOL OR (ISO
             OR 2)()PROPANOL OR ISOPROPANOL OR DIMETHYLCARBINOL OR IPA
S3     212398   HEPATITIS OR CIRRHOSIS OR RIFT()VALLEY()FEVER
S4      74684   CHIARI? ?()SYNDROME OR HEPATIC()VEIN()THROMBOSIS OR HEPATO-
             CELLULAR(N)CARCINOMA? ? OR HEPATOMA OR PORTOSYSTEMIC()ENCEPHA-
             LOPATHY
S5     340514   HEPATIC OR LIVER(1N)(DISEASE? ? OR NECROSIS OR TUMOR? ? OR
             TUMOUR? ? OR CANCER? ? OR NEOPLASM? ?) OR HEPATOTOXICITY
S6     635274   LIVER
S7     122160   BREATH? OR EXPIRATORY OR EXHAL? OR EXPIRATION
S8          7   S1:S2 AND S3:S6 AND S7
S9          6   RD (unique items)
S10      1611   S1:S2 AND S3:S6
S11        65   DIAGNOS? AND S10
S12     46307   RESPIRATORY()AIR OR EXPIR?
S13         0   S11 AND S12
S14     40109   S7 AND S12
S15         2   S7 AND S11 [duplicates]
```

9/7/3 (Item 3 from file: 34)

```
DIALOG(R)File  34:SciSearch(R) Cited Ref Sci
(c) 2005 Inst for Sci Info. All rts. reserv.
07952497   Genuine Article#: 228KL   Number of References: 35
```

Title: Metabolic activation of dacarbazine by human cytochromes P450: The role of CYP1A1, CYP1A2, and CYP2E1

```
Author(s): Reid JM (REPRINT) ; Kuffel MJ; Miller JK; Rios R; Ames MM
Corporate Source: MAYO CLIN,DEPT ONCOL, DIV DEV ONCOL RES, 200 1ST ST
    SW/ROCHESTER//MN/55905 (REPRINT)
Journal: CLINICAL CANCER RESEARCH, 1999, V5, N8 (AUG), P2192-2197
ISSN: 1078-0432   Publication date: 19990800
Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202
Language: English   Document Type: ARTICLE
Abstract: Dacarbazine (DTIC), a widely used anticancer agent, is inactive
    until metabolized in the liver by cytochromes P450 to form the
    reactive N-demethylated species
    5-[3-hydroxymethyl-3-methyl-triazen-1-yl]-imidazole- (HMMTIC) and
    5-[3-methyl-triazen-1-yl]-imidazole-4-carboxamide (MTIC). The modest
    activity of DTIC in the treatment of cancer patients has been
    attributed in part to lower activity of cytochromes P450 (P450) in
    humans when compared with rodents. Importantly, the particular P450
    isoforms involved in the activation pathway have not been reported. We
```

now report that the DTIC N-demethylation involved in MTIC formation by human **liver** microsomes is catalyzed by CYP1A1, CYP1A2, and CYP2E1, The most potent inhibitors of DTIC N-demethylation were alpha-naphthoflavone (CYP1A1 and CYP1A2), quercetin (CYP1A2), chlorzoxazone (CYP1A2 and CYP2E1), and di-sulfiram (CYP2E1). Antihuman CYP1A2 antiserum also inhibited DTIC N-demethylation, DTIC N-demethylation in a panel of 10 human **liver** microsome preparations was correlated with the catalytic activities for CYP1A2 (ethoxyresorufin O-deethylation and caffeine N-3-demethylation) in the absence of alpha-naphthoflavone and with the catalytic activities for CYP2E1 (chlorzoxazone 6-hydroxylations) in the presence of **cn** -naphthoflavone. DTIC metabolism was catalyzed by recombinant human CYP1A1, CYP1A2, and CYP2E1. The K-m (V-max) values for metabolism of DTIC by recombinant human CYP1A1 and CYP1A2 were 595 mu M (0.684 nmol/min/mg protein) and 659 mu M (1.74 nmol/min/mg protein), respectively. The CYP2E1 K(m) value exceeded 2.8 mM. Thus, we conclude that (a) CYP1A2 is the predominant P450 that catalyzes DTIC **hepatic** metabolism; (b) CYP2E1 contributes to **hepatic** DTIC metabolism at higher substrate concentrations; and (c) CYP1A1 catalyzes **extrahepatic** metabolism of DTIC.

9/7/4 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03436422 Genuine Article#: PE844 Number of References: 25
Title: ACUTE PERCUTANEOUS SYSTEMIC TOXICITY OF CYANIDES
Author(s): BALLANTYNE B
Corporate Source: UNION CARBIDE CORP,DEPT APPL TOXICOL,39 OLD RIDGEBURY RD/DANBURY//CT/06817
Journal: JOURNAL OF TOXICOLOGY-CUTANEOUS AND OCULAR TOXICOLOGY, 1994, V13, N3, P249-262
ISSN: 0731-3829
Language: ENGLISH Document Type: ARTICLE
Abstract: The acute percutaneous systemic toxicity of hydrogen (HCN), sodium (NaCN), and potassium **cyanides** (KCN) was investigated in female albino rabbits. LD(50) values (with 95% confidence limits), in mmol/kg, for solutions applied to intact skin were 0.260 (0.238-0.278) for HCN, 0.299 (0.282-0.315) for NaCN, and 0.344 (0.315-0.369) for KCN. The corresponding values for solutions applied to abraded skin were 0.087 (0.076-0.097), 0.231 (0.188-0.259), and 0.220 (0.204-0.233). NaCN powder applied at 200 mg/kg to dry intact skin did not produce death or signs, and applied to intact moist skin it gave an LD(50) of 0.243 (0.152-0.388) mmol/kg and NaCN powder applied to abraded skin gave an LD(50) of 0.151 (0.137-0.160) mmol/kg. For each application condition there was a wide range of times to onset of signs and times to death. Mean times to death were shortest with NaCN powder applied to abraded skin (44.5 min) and longest with NaCN solution applied to intact skin (252.1 min). Signs, seen mainly in animals that died, included tremors, retrocolic spasms, convulsions, abnormal **breathing** patterns, and prostration. In a follow-up investigation, **cyanide** was measured in blood, serum, and various tissues removed immediately after death following epicutaneous dosing with solutions of HCN, NaCN, or KCN to intact rabbit skin at 35 mg **CN** /kg (i.e., 3.9-5.3 x LD(50)). High **cyanide** concentrations were measured in whole blood and serum from all groups, and detected analytically in heart, **liver** , kidney, spleen, lung, brain, and spinal cord. Highest average tissue concentrations

were measured in heart, kidney, brain, and lung. Lowest individual concentrations were in **liver** . These results indicate a potential for acute lethal toxicity by single sustained contact of **cyanide** solutions with intact skin, or NaCN powder on moist skin. Lethal toxicity (as LD(50)) is enhanced by skin injury. There are clear indications for the use of protective measures when handling **cyanide** .

9/7/6 (Item 1 from file: 144)

14849211 PASCAL No.: 00-0533899

Simvastatin does not affect CYP3A activity, quantified by the erythromycin breath **test and oral midazolam pharmacokinetics, in healthy male subjects**

PRUEKSARITANONT Thomayant; VEGA Jose M; ROGERS J Douglas; GAGLIANO Kathleen; GREENBERG Howard E; GILLEN Lisa; BRUCKER Mary Jo; MCLOUGHLIN Debra; WONG Peggy H; WALDMAN Scott A

Merck Research Laboratory, Blue Bell and, West Point, Pennsylvania, United States; Merck Research Laboratory, Rahway, New Jersey, United States ; Thomas Jefferson University, Philadelphia, Pennsylvania, United States

Journal: Journal of clinical pharmacology, 2000, 40 (11) 1274-1279
ISSN: 0091-2700 CODEN: JCPCBR Availability: INIST-10257; 354000092636260090
No. of Refs.: 18 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: United States
Language: English

Potential for inhibition of CYP3A activity by simvastatin, an HMG-CoA reductase inhibitor, was evaluated in 12 healthy male subjects who received placebo or 80 mg of simvastatin, the maximal recommended dose, once daily for 7 consecutive days. On day 7, an intravenous injection of 3 mu Ci (SUP 1 SUP 4 **CN** -methyl)erythromycin for the erythromycin **breath** test (EBT) was coadministered with a 2 mg oral solution of midazolam. The values for percent SUP 1 SUP 4 C **exhaled** during the first hour (for EBT) and the pharmacokinetic parameters of midazolam (AUC, C SUB m SUB a SUB x , t SUB 1 SUB / SUB 2) were not affected following multiple once-daily oral doses of simvastatin 80 mg. The 95% confidence interval was 0.97 to 1.18 for EBT and 0.99 to 1.23 for midazolam AUC. In addition, the total urinary recoveries of midazolam and its 1'-hydroxy metabolites (free plus conjugate) obtained from both treatments were not statistically different ($p > 0.200$). These data demonstrate that multiple dosing of simvastatin, at the highest recommended clinical dose, does not significantly alter the in vivo **hepatic** or intestinal CYP3A4/5 activity as measured by the commonly used EBT and oral midazolam probes.

FILE 'HCAPLUS, BIOSIS, EMBASE' ENTERED AT 15:30:39 ON 09 NOV 2005
L1 1 S CYANIDE/CN
L2 1 S ISOPROPANOL/CN
L3 209816 S CYANIDE# OR ISOCYANIDE# OR CYANAMIDE# OR FERROCYANIDE# OR FER
L4 21894 S L1
L5 89854 S ISOPROPANOL OR ISOPROPYL ALCOHOL OR 2()PROPANOL OR L2
L6 233301 S HEPATOCELLULAR CARCINOMA# OR HEPATOMA OR HEPATIC ENCEPHALOPAT
L7 350709 S HEPATITIS OR RIFTVALLEY FEVER OR CIRRHOSIS OR CHIARI#()SYNDR
L8 1756329 S LIVER OR HEPATIC OR HEPATO?
L9 53356 S BREATH OR EXPIRATION
L10 350 S BREATHALYZER# OR BREATHALYSER#
L11 18 S (L3 OR L4 OR L5) AND (L6 OR L7 OR L8) AND (L9 OR L10)
L12 13 DUPLICATE REMOVE L11 (5 DUPLICATES REMOVED)

L12 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:149514 HCAPLUS
DN 137:352752
ED Entered STN: 27 Feb 2002
TI Synthesis of 14C-labeled lidocaine (2-diethylamino)-N-(2,6-dimethylphenyl)acetamide
AU Zhou, Zhentang; Qian, Guojun; Lin, Fenzhi; Zhuang, Daoling; Zhang, Yulong; He, Zhanjun
CS Shanghai Institute of Nuclear Research, Chinese Academy of Science, Shanghai, 201800, Peop. Rep. China
SO Hejishu (2002), 25(1), 54-56
CODEN: NUTEDL; ISSN: 0253-3219
PB Kexue Chubanshe
DT Journal
LA Chinese
CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 8
OS CASREACT 137:352752
AB 14C-lidocaine was synthesized from 14C-diethylamine reaction with .omega.-chloroacetic-2,6-dimethylaniline. 14C-diethylamine was prepd. from Ba14CO3 via K14CN and 14C-acetanitrile which was hydrogenated. Radiochem. purity of 14C-diethylamine and 14C-lidocaine is >99% by HPLC and TLC resp. 14C-lidocaine is needed for ***breath*** assay of mouse for measuring ***liver*** function.
ST C14 labeled lidocaine synthesis isotope indicator tracer
IT Isotope indicators
(synthesis of 14C-labeled lidocaine)
IT 474477-44-6P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(of synthesis 14C-labeled)
IT 74-88-4, Methyl iodide, reactions 1131-01-7 1882-53-7 26628-22-8, Sodium azide
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of 14C-labeled lidocaine)
IT 5373-08-0P, Potassium ***cyanide*** (K(14CN)) 7183-56-4P, Acetonitrile-1-14C 474477-39-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of 14C-labeled lidocaine)

L12 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:25616 HCAPLUS
DN 134:83064
ED Entered STN: 11 Jan 2001
TI Methods of use for sensor-based fluid detection devices
IN Lewis, Nathan S.
PA California Institute of Technology, USA
SO U.S., 48 pp., Cont.-in-part of U.S. 6,010,616.
CODEN: USXXAM
DT Patent
LA English
IC ICM G01N033-497
ICS G01N027-00; G08B017-10
INCL 073023340
CC 9-1 (Biochemical Methods)
Section cross-reference(s): 4, 17, 59, 63, 80
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6170318	B1	20010109	US 1998-183724	19981030
	US 5571401	A	19961105	US 1995-410809	19950327
	EP 950895	A2	19991020	EP 1999-202573	19960326
	EP 950895	A3	20020102		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 5698089	A	19971216	US 1996-689227	19960807
	US 6010616	A	20000104	US 1997-986500	19971208
	US 5951846	A	19990914	US 1998-6142	19980114
	US 6013229	A	20000111	US 1998-95376	19980610
	US 5891398	A	19990406	US 1998-154604	19980916
	US 6017440	A	20000125	US 1998-209914	19981211
	US 6093308	A	20000725	US 1999-258713	19990226
	WO 2000026638	A1	20000511	WO 1999-US25544	19991029
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1131616	A1	20010912	EP 1999-956803	19991029
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002529694	T2	20020910	JP 2000-579968	19991029
	US 6331244	B1	20011218	US 2000-478680	20000106
	US 2004033165	A1	20040219	US 2003-409449	20030407
PRAI	US 1995-410809	A1	19950327		
	US 1996-689227	A1	19960807		
	US 1997-986500	A2	19971208		
	EP 1996-910563	A3	19960326		
	US 1996-696128	A1	19960814		
	US 1997-949730	A1	19971014		
	US 1998-6142	A1	19980114		
	US 1998-183724	A	19981030		
	US 1998-209914	A1	19981211		
	US 1999-258713	A1	19990226		

US 1999-369507 B1 19990806
WO 1999-US25544 W 19991029

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6170318	ICM	G01N033-497
	ICS	G01N027-00; G08B017-10
	INCL	073023340
US 6170318	NCL	073/023.340; 340/632.000; 422/098.000
	ECLA	G01N027/12D; G01N033/00D2D2; G01N033/497; G01N033/497A
US 5571401	NCL	205/787.000; 204/406.000; 204/415.000; 204/418.000; 205/775.000; 205/782.500; 422/068.100; 422/069.000; 422/082.010; 422/082.020; 422/083.000; 422/098.000; 436/150.000
	ECLA	G01N027/12D; G01N033/00D2D2
EP 950895	ECLA	G01N027/12D; G01N033/00D2D2
US 5698089	NCL	205/787.000; 204/406.000; 204/416.000; 204/418.000; 205/775.000; 205/782.500; 422/068.100; 422/069.000; 422/082.010; 422/082.020; 436/150.000
	ECLA	G01N027/12D; G01N033/00D2D2
US 6010616	NCL	205/787.000; 073/023.200; 073/023.310; 073/023.340; 073/335.050; 204/406.000; 204/415.000; 204/418.000; 205/775.000; 205/782.500; 324/691.000; 324/693.000; 338/007.000; 338/013.000; 338/014.000; 422/082.020; 422/082.120; 422/098.000; 436/150.000
	ECLA	G01N027/12D; G01N033/00D2D2
US 5951846	NCL	205/787.000; 073/023.200; 073/023.310; 073/023.340; 073/335.050; 204/406.000; 204/415.000; 204/418.000; 205/775.000; 205/782.500; 324/691.000; 324/693.000; 338/007.000; 338/013.000; 338/014.000; 422/082.010; 422/082.020; 422/098.000; 436/150.000; 436/151.000
	ECLA	G01N027/12D; G01N033/00D2D2
US 6013229	NCL	422/082.020; 204/418.000; 422/068.100; 422/069.000; 422/082.010; 422/088.000; 422/098.000; 436/150.000
	ECLA	G01N027/12D; G01N033/00D2D2
US 5891398	NCL	422/082.020; 073/023.200; 073/023.310; 073/023.340; 073/335.050; 204/406.000; 204/415.000; 204/418.000; 324/691.000; 324/693.000; 338/007.000; 338/013.000; 338/014.000; 422/098.000; 436/149.000; 436/150.000
	ECLA	G01N027/12D; G01N033/00D2D2
US 6017440	NCL	205/777.500; 204/403.010; 204/403.060; 204/403.150; 204/406.000; 204/415.000; 204/418.000; 205/778.000; 435/289.100; 435/817.000
	ECLA	G01N027/12D; G01N033/00D2D2
US 6093308	NCL	205/787.000; 073/023.200; 073/023.310; 073/023.340; 073/335.050; 204/406.000; 204/415.000; 204/418.000; 205/775.000; 205/782.500; 324/691.000; 324/693.000; 338/007.000; 338/013.000; 338/014.000; 422/082.020; 422/082.120; 422/098.000; 436/150.000
	ECLA	G01N027/12D; G01N033/00D2D2
WO 2000026638	ECLA	G01N027/12D; G01N033/00D2D2; G01N033/497; G01N033/497A
US 6331244	NCL	205/777.500; 422/082.010; 422/082.020; 436/150.000
	ECLA	G01N027/12D; G01N033/00D2D2
US 2004033165	NCL	422/082.020
	ECLA	G01N027/12D; G01N033/00D2D2

AB Methods of use and devices for detecting analyte in fluid are described. A system for detecting an analyte in a fluid is described comprising a

substrate having a sensor comprising a first org. material and a second org. material where the sensor has a response to permeation by an analyte. A detector is operatively assocd. with the sensor. Further, a fluid delivery appliance is operatively assocd. with the sensor. The sensor device has information storage and processing equipment, which is operably connected with the device. This device compares a response from the detector with a stored ideal response to detect the presence of analyte. An integrated system for detecting an analyte in a fluid is also described where the sensing device, detector, information storage and processing device, and fluid delivery device are incorporated in a substrate. Methods for use for the above system are also described where the first org. material and a second org. material are sensed and the analyte is detected with a detector operatively assocd. with the sensor. The method provides for a device, which delivers fluid to the sensor and measures the response of the sensor with the detector. Further, the response is compared to a stored ideal response for the analyte to det. the presence of the analyte. In different embodiments, the fluid measured may be a gaseous fluid, a liq., or a fluid extd. from a solid. Methods of fluid delivery for each embodiment are accordingly provided. The sensor assembly is used to detect analytes indicative of disease, of exposure to toxic substances, of spoiled food, of air quality, of noxious poisonous vapors, etc. The sensor may be incorporated into bandages.

ST sensor based fluid analysis app

IT Polysulfones, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(as nonconductive polymer with carbon black-based sensor; methods of use for sensor-based fluid detection devices)

IT Polycarbonates, uses
Polyvinyl butyrals
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(as plasticizer; methods of use for sensor-based fluid detection devices)

IT Medical goods
(bandages, sensor in; methods of use for sensor-based fluid detection devices)

IT Toxoids
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(botulin, detection of analyte indicative of; methods of use for sensor-based fluid detection devices)

IT Respiratory air
(***breath**alyzers*** ; methods of use for sensor-based fluid detection devices)

IT Diagnosis
(cancer, detection of analyte indicative of; methods of use for sensor-based fluid detection devices)

IT Sensors
(conductometric; methods of use for sensor-based fluid detection devices)

IT Toxins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(detection of analyte indicative of exposure to; methods of use for sensor-based fluid detection devices)

IT Cooking

(detection of analyte indicative of food; methods of use for sensor-based fluid detection devices)
IT Fish
(detection of analyte indicative of freshness of; methods of use for sensor-based fluid detection devices)
IT Beverages
(detection of analyte indicative of quality control in food or; methods of use for sensor-based fluid detection devices)
IT Dairy products
(detection of analyte indicative of spoilage of; methods of use for sensor-based fluid detection devices)
IT Escherichia coli
Hazardous materials
Liver , ***disease***
Salmonella
(detection of analyte indicative of; methods of use for sensor-based fluid detection devices)
IT Diabetes mellitus
(detection of ketone levels indicative of; methods of use for sensor-based fluid detection devices)
IT Neoplasm
(diagnosis, detection of analyte indicative of; methods of use for sensor-based fluid detection devices)
IT Kidney, disease
(failure, detection of analyte indicative of; methods of use for sensor-based fluid detection devices)
IT Poisons, nonbiological source
(gaseous, detection of analyte indicative of; methods of use for sensor-based fluid detection devices)
IT Ketones, analysis
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(in diabetes mellitus; methods of use for sensor-based fluid detection devices)
IT Skin, disease
(infection, bacterial, detection of analyte indicative of; methods of use for sensor-based fluid detection devices)
IT Electrodes
(interdigitated and coated; methods of use for sensor-based fluid detection devices)
IT Air analysis
Analytical apparatus
Biosensors
Blood analysis
Diagnosis
Environmental analysis
Fluids
Gas analysis
Principal component analysis
Sensors
Vapors
(methods of use for sensor-based fluid detection devices)
IT Ulcer
(peptic, detection of analyte indicative of; methods of use for sensor-based fluid detection devices)
IT Carbon black, uses
RL: DEV (Device component use); USES (Uses)

(sensors based on; methods of use for sensor-based fluid detection devices)
IT Food analysis
(spoiled food detection; methods of use for sensor-based fluid detection devices)
IT Sensors
(voltammetric sensors; methods of use for sensor-based fluid detection devices)
IT 9003-22-9 24979-70-2, Poly(4-vinyl phenol) 25037-45-0, Poly(bisphenol A carbonate)
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(as nonconductive polymer with carbon black-based sensor; methods of use for sensor-based fluid detection devices)
IT 9003-20-7, Polyvinyl acetate 9003-39-8, Poly(vinyl pyrrolidone) 9003-53-6, Polystyrene 9003-54-7, Poly(styrene-acrylonitrile) 9011-13-6, Poly(styrene-maleic anhydride) 25014-31-7, Poly(.alpha.-methyl styrene) 25119-62-4, Poly(styrene-allyl alcohol) 59269-51-1, Polyvinyl phenol
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(as plasticizer; methods of use for sensor-based fluid detection devices)
IT 64-17-5, Ethanol, analysis
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(detection of analyte indicative of intoxication with; methods of use for sensor-based fluid detection devices)
IT 67-56-1, Methanol, analysis ***67-63-0*** , ***Isopropyl*** ***alcohol*** , analysis 67-64-1, Acetone, analysis 67-66-3, Chloroform, analysis 71-43-2, Benzene, analysis 108-88-3, Toluene, analysis 109-99-9, Tetrahydrofuran, analysis 110-54-3, Hexane, analysis 141-78-6, Ethyl acetate, analysis
RL: ANT (Analyte); ANST (Analytical study)
(methods of use for sensor-based fluid detection devices)
IT 30604-81-0P, Poly(pyrrole)
RL: ARG (Analytical reagent use); DEV (Device component use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(methods of use for sensor-based fluid detection devices)
IT 12026-57-2, Phosphomolybdic acid
RL: CAT (Catalyst use); USES (Uses)
(methods of use for sensor-based fluid detection devices)

L12 ANSWER 3 OF 13 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
AN 2000011277 EMBASE
TI Measurement of exhaled nitric oxide in humans and animals.
AU Bernareggi M.; Cremona G.
CS G. Cremona, Respiratory Medical Unit, Scientific Institute San Raffaele, Via Olgettina 60, 20132 Milano, Italy
SO Pulmonary Pharmacology and Therapeutics, (1999) Vol. 12, No. 6, pp. 331-352.
Refs: 205
ISSN: 1094-5539 CODEN: PPTHFJ

CY United Kingdom
DT Journal; General Review
FS 002 Physiology
030 Pharmacology
037 Drug Literature Index
LA English
ED Entered STN: 20000113
Last Updated on STN: 20000113
CT Medical Descriptors:
*expired air
****breath analysis***
respiratory epithelium
chemoluminescence
tidal volume
spirometry
breath holding
food intake
beverage
circadian rhythm
gender
smoking
exercise
experimental model
compartment model
asthma: DI, diagnosis
asthma: DT, drug therapy
allergy: DI, diagnosis
allergy: ET, etiology
bronchoscopy
bronchiectasis: DT, drug therapy
cystic fibrosis: ET, etiology
chronic obstructive lung disease: ET, etiology
lung cancer: ET, etiology
lung transplantation
cardiovascular disease: DT, drug therapy
cardiovascular disease: ET, etiology
cardiopulmonary bypass
infection: ET, etiology
liver cirrhosis: ET, etiology
sleep apnea syndrome: ET, etiology
human
nonhuman
review
priority journal
Drug Descriptors:
*nitric oxide: EC, endogenous compound
nitric oxide synthase: EC, endogenous compound
glucocorticoid: DT, drug therapy
steroid: DT, drug therapy
n(g) nitroarginine methyl ester: DT, drug therapy
n(g) methylarginine: DT, drug therapy
arginine: DT, drug therapy
glyceryl trinitrate: DT, drug therapy
nitroprusside sodium: DT, drug therapy
RN (Nitric Oxide) 10102-43-9; (nitric oxide synthase) 125978-95-2; (n(g) nitroarginine methyl ester) 50903-99-6; (n(g) methylarginine) 156706-47-7, 17035-90-4; (arginine) 1119-34-2, 15595-35-4, 7004-12-8, 74-79-3;

(glyceryl trinitrate) 55-63-0; (***nitroprusside*** sodium). 14402-89-2, 15078-28-1

L12 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

AN 1990:587304 HCAPLUS

DN 113:187304

ED Entered STN: 23 Nov 1990

TI Bioavailability of iron and ***cyanide* from iron-59- and carbon-14-labeled hexacyanoferrates(II) in rats**

AU Nielsen, Peter; Dresow, Bernd; Fischer, Roland; Heinrich, Hellmuth C.

CS Inst. Physiol. Chem., Universitaetskrankenhaus Eppendorf, Hamburg, 2000/20, Germany

SO Zeitschriftfuer Naturforschung, C: Journal of Biosciences (1990), 45(6), 681-90
CODEN: ZNCBDA; ISSN: 0341-0382

DT Journal

LA English

CC 8-6 (Radiation Biochemistry)

AB "Sol." (KFeIII[FeII(CN)6]) and "insol. Prussian blue" (FeIII4[FeII(CN)6]3) labeled with 59Fe either in the ferric (FeIII) or ferro (FeII) position and 14C in the ***cyanide*** group were synthesized and administered i.p. or orally to adult female rats with normal body Fe stores. Following i.p. injection of KFe[Fe(CN)6], the colloidal complex is disintegrated into ferric iron and hexacyanoferrate(II) anion almost completely. About 96% of the ferric iron was retained in the body. Nearly 90% of both ferrous iron and ***cyanide*** were excreted with the urine within 7 days after i.p. injection, indicating that most of the undissociated hexacyanoferrate(II) anion ([Fe(CN)6]4-) was excreted through the kidney. Only 9% of the ferrous iron from [Fe(CN)6]4- was found mainly in carcass, ***liver*** , and gut. As the 59Fe/14C-ratios in organs were found close to 1.0, the dissocn. of the hexacyanoferrate(II) anion can only be small in vivo. No detectable 14CO2-activity (<0.01%) was monitored in the ***breath*** of rats after i.p. injection of the 14C-labeled KFe[Fe(CN)6], also indicating that no significant amts. of ***cyanide*** were released after parenteral administration. After oral administration of the sol. and insol. Prussian blue, 0.3-0.7% of the ferric iron was absorbed and retained mainly in carcass, ***liver*** , and blood. Only 0.06-0.18% of the ferrous iron was absorbed and mostly excreted with the urine (0.05-0.15%), so that only 0.01-0.03% of the oral ferrous 59Fe was retained in the body after 7-10 days. Very small fractions of 14C-label from the 14CN-group of the sol. and insol. hexacyanoferrate(II) were obsd. in the exhaled air (0.04-0.08% of the oral dose). From the 14CO2-exhalation, the 14C urine excretion and the distribution of Fe in blood and organs, it can be concluded that the hexacyanoferrate(II) moiety disintegrated only to a small extent in the intestinal tract after oral administration. From a dose of 36 mg hexacyanoferrate(II)/kg, an amt. of free (noncomplex bound) ***cyanide*** can be calcd. which is in max. 2 orders of magnitude below the LD100-level. Thus, the very low bioavailability of Fe and ***cyanide*** from hexacyanoferrate(II) compds. after oral application is demonstrated in rats. In the case of a severe nuclear accident, appropriate doses of "sol." and "insol." Prussian blue can be used as a safe and effective antidote against radiocesium contamination.

ST hexacyanoferrate iron ***cyanide*** bioavailability; radiocesium decorporation Prussian blue

IT Organ

(hexacyanoferrates metab. and biodistribution in, tracer studies of, radiocesium decorporation in relation to)
IT ***57-12-5*** , ***Cyanide*** , biological studies 7439-89-6, Iron, biological studies
RL: BIOL (Biological study)
(bioavailability of, from hexacyanoferrates, radiocesium decorporation in relation to)
IT 10045-97-3, Cesium-137, biological studies 13967-70-9, Cesium-134, biological studies
RL: BIOL (Biological study)
(decorporation of, with Prussian blue, ***cyanide*** and iron bioavailability in relation to)
IT 151-50-8, Potassium ***cyanide*** (K(CN))
RL: BIOL (Biological study)
(in hexacyanoferrate prepn.)
IT 14038-43-8 25869-98-1
RL: BIOL (Biological study)
(metab. of and ***cyanide*** and iron bioavailability from, radiocesium decorporation in relation to)
IT 129889-68-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction with iron trichloride)
IT 130140-13-5P 130140-14-6P 130140-15-7P 130160-33-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT 14596-12-4, Iron-59, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with ferrous sulfate and ***cyanide***)
IT 10025-77-1, Ferric trichloride hexahydrate 18497-67-1, Iron chloride (59FeCl3)
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with hexacyanoferrate)
IT 7720-78-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with iron-59 ***cyanide***)
IT 129889-69-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with iron-59 trichloride)

L12 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1988:199649 HCAPLUS
DN 108:199649
ED Entered STN: 11 Jun 1988
TI The possible role of the ethanol-inducible isozyme of cytochrome P 450 in the metabolism and distribution of carbon disulfide
AU Snyderwine, Elizabeth G.; Kroll, Rosanna; Rubin, Robert J.
CS Sch. Hyg. Public Health, Johns Hopkins Univ., Baltimore, MD, 21205, USA
SO Toxicology and Applied Pharmacology (1988), 93(1), 11-21
CODEN: TXAPA9; ISSN: 0041-008X
DT Journal
LA English
CC 4-3 (Toxicology)
AB The ability of several different alcs. to induce the ***hepatic*** mixed-function oxidase (MFO) metab. of CS2 and the effects of this induction on CS2 distribution and ***hepato***toxicity*** were examd. in

rats. Eighteen hours after alc. administration (1/2 LD50 dose, orally), CS2 microsomal MFO metab. was significantly enhanced, in order of descending potency, by ***isopropanol*** , MeOH and EtOH pretreatments, but not by isobutanol pretreatment. The degree of enhancement of CS2 metab. by different alcs. paralleled the enhancement of nitroanisole-O-demethylation and aniline hydroxylation, MFO activities assocd. with the EtOH-inducible isoenzyme of cytochrome P 450. CS2 (1 mg/kg, i.p. 3 h) inhibited only the cytochrome P 450-mediated activities enhanced by alc. pretreatment. Apparently, CS2 metab. is catalyzed by the EtOH-inducible isoenzyme. Alc.-induced rats had significantly more 14CS2-derived radioactivity in the ***liver*** than control and isobutanol-pretreated rats 3 h after dosing (1 mg/kg, i.p.). However, only MeOH pretreatment resulted in an increased retention of 14CS2-derived radioactivity in plasma, brain, and kidney. Unlike other alc. pretreatments, MeOH decreased the total 14C expired during the 3-h period after CS2 dosing and caused a significant (2-fold) increase in plasma glutamic-pyruvic transaminase, measured 24 h after CS2 exposure (625 mg/kg). Thus, alc. induction of MFO-dependent CS2 metab. per se is not sufficient to result in CS2-induced ***hepatic*** damage although it does lead to loss of specific cytochrome P 450 function.

ST alc carbon disulfide metab toxicity; ***hepatotoxicity*** carbon disulfide alc; ethanol cytochrome P 450 carbon disulfide

IT Blood plasma
Brain, metabolism
Kidney, metabolism
Organ
(carbon disulfide distribution in, after administration, aliph. alcs. effect on)

IT Air, respiratory
(carbon disulfide of, after administration, aliph. alcs. effect on)

IT ***Liver*** , toxic chemical and physical damage
(carbon disulfide toxicity to, aliph. alcs. effect on)

IT Microsome
(mixed-function oxidase system of ***liver*** , carbon disulfide effect on, after ***isopropanol*** treatment)

IT Enzymes
RL: BIOL (Biological study)
(of ***liver*** , aliph. alcs. effect on, carbon disulfide metab. in relation to)

IT Alcohols, biological studies
RL: BIOL (Biological study)
(aliph., carbon disulfide metab. and toxicity response to, ***hepatic*** mixed-function oxidase metab. in relation to)

IT 64-17-5, Ethanol, biological studies 67-56-1, Methanol, biological studies ***67-63-0*** , ***Isopropanol*** , biological studies 78-83-1, Isobutanol, biological studies
RL: BIOL (Biological study)
(carbon disulfide metab. and toxicity response to, ***hepatic*** mixed-function oxidase metab. in relation to)

IT 9035-51-2, Cytochrome P 450, biological studies
RL: BIOL (Biological study)
(ethanol-inducible isoenzyme of, in carbon disulfide metab.)

IT 124-38-9, Carbon dioxide, biological studies
RL: BIOL (Biological study)
(***expiration*** of, after carbon disulfide administration, aliph. alcs. effect on)

IT 75-15-0, Carbon disulfide, biological studies

RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metab. and toxicity of, in ***liver*** , aliph. alcs. effect on)
IT 9000-86-6, Glutamic-pyruvic transaminase
RL: BIOL (Biological study)
(of blood plasma, during carbon disulfide ***hepatotoxicity*** , aliph. alcs. effect on)
IT 463-58-1, Carbonyl sulfide 9012-80-0, Aniline hydroxylase 9037-69-8, Aminopyrine N-demethylase 9038-14-6, Mixed-function oxidase 9054-86-8, 4-Nitroanisole O-demethylase
RL: BIOL (Biological study)
(of ***liver*** , aliph. alcs. effect on, carbon disulfide metab. in relation to)

L12 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1987:613158 HCAPLUS
DN 107:213158
ED Entered STN: 12 Dec 1987
TI Metabolism of selenocyanate in the rat
AU Vadhanavikit, Surasi; Kraus, Richard J.; Ganther, Howard E.
CS Dep. Nutr. Sci., Univ. Wisconsin, Madison, WI, 53706, USA
SO Archives of Biochemistry and Biophysics (1987), 258(1), 1-6
CODEN: ABBIA4; ISSN: 0003-9861
DT Journal
LA English
CC 4-3 (Toxicology)
AB Rats injected s.c. with 2 mg Se/kg (as [75Se]selenocyanate or [14C,75Se]selenocyanate) excreted dimethylselenide (DMSe) in the ***breath*** and trimethylselenonium ion (TMSe) in the urine. The 24-h respiratory DMSe and urinary TMSe excretions were 26.8 and 14.5 % of the dose, resp. Tissue concns. of 75Se were highest in the kidneys (1.89 % dose/g), ***liver*** (1.46 % dose/g), and blood (0.50 % dose/mL), and lower (<0.3% dose/g) in the other tissues. TMSe was the major form (61%) of Se in urine. Approx. 2% of the dose od doubly labeled SeCN- was excreted unchanged in urine (.apprx.12% of urinary Se). 14C from doubly labeled SeCN- was not present in the methylated Se metabolites, but a major 14C urinary metabolite was identified as thiocyanate. Apparently, a substantial part of selenocyanate in the body undergoes metab. and Se is excreted in methylated forms following scission of the C-Se bond.
ST selenocyanate metab selenium detoxication
IT Air, respiratory
(dimethylselenide of, after selenocyanate administration)
IT Detoxication
(of selenium, selenocyanate metab. in relation to)
IT Blood
Kidney, composition
Liver , composition
(selenium of, after selenocyanate administration)
IT Urine
(trimethylsilonium ion of, after selenocyanate administration)
IT 7782-49-2, Selenium, biological studies
RL: BIOL (Biological study)
(detoxication of, selenocyanate metab. in relation to)
IT 593-79-3, Dimethylselenide
RL: PROC (Process)

(excretion of, in respiratory air)
IT 5749-48-4, Selenocyanate
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metab. of, selenium detoxication in relation to)
IT 302-04-5, Thiocyanate ion, biological studies 25930-79-4, Trimethylselenium ion
RL: BIOL (Biological study)
(of urine, after selenocyanate administration)
IT 111317-56-7P 111317-57-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT 20324-16-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with potassium ***cyanide***)
IT 151-50-8 5373-08-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with selenious acid labeled with selenium 75)

L12 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
AN 1982:521513 HCAPLUS
DN 97:121513
ED Entered STN: 12 May 1984
TI ***Isopropanol* enhancement of carbon tetrachloride metabolism in vivo**
AU Reynolds, Edward S.; Moslen, Mary Treinen; Treinen, Richard J.
CS Med. Branch, Univ. Texas, Galveston, TX, 77550, USA
SO Life Sciences (1982), 31(7), 661-9
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
CC 4-3 (Toxicology)
AB The effects of ***isopropanol*** (ISOP) [***67-63-0***] pretreatment on the metab. of 14C-labeled CCl4 [56-23-5] to 14CO2 and CHCl3 [67-66-3] exhaled in the ***breath*** to 14C metabolite excreted in 24 h urine and feces from 0 to 24 h, and to 14C metabolite bound to ***liver*** at 24 h was examd. Fasted male rats were given 0.1 or 2.0 mmoles 14CCl4/kg. ISOP pretreatment, which enhanced the ***hepatotoxicity*** of CCl4, selectivity enhanced the rate and total extent of 14CO2 and CHCl3 metabolite exhalation. The pathways of CCl4 metab. leading to CO2 and CHCl3 metabolite formation may be more relevant to the ***hepatotoxicity*** of CCl4 than the pathways leading to urinary, fecal or covalently bound metabolites.
ST ***isopropanol*** carbon tetrachloride metab
IT ***Liver*** , metabolism
(carbon tetrachloride metab. by, ***isopropanol*** effect on)
IT 67-66-3, biological studies 124-38-9, biological studies
RL: BIOL (Biological study)
(as carbon tetrachloride metabolite, ***isopropanol*** effect on)
IT ***67-63-0*** , biological studies
RL: BIOL (Biological study)
(carbon tetrachloride metab. enhancement by)
IT 56-23-5, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metab. of, ***isopropanol*** enhancement of)

L12 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1983:465616 HCAPLUS
DN 99:65616
ED Entered STN: 12 May 1984
TI Metabolism of 1-propyl-1-nitrosourea (PNU) in rats
AU Tanaka, A.; Watanabe, M.
CS Div. Med. Chem., Natl. Inst. Hyg. Sci., Tokyo, 158, Japan
SO IARC Scientific Publications (1982), 41(N-Nitroso Compd: Occurrence Biol. Eff.), 483-91
CODEN: IARCCD; ISSN: 0300-5038
DT Journal
LA English
CC 4-6 (Toxicology)
AB The carcinogen, 14C-labeled 1-propyl-1-nitrosourea (PNU) [816-57-9], was absorbed from the rat gut and the radioactivity excreted mainly in the urine and **expired** air. The urinary metabolites of PNU were 1-propylurea (PU) [627-06-5] and urea [57-13-6]. The metabolite PU was excreted largely unchanged in the urine. [14C]PNU and [14C]PU were eliminated rapidly from the rat body. In addn. to CO2 from PNU, ***isopropanol*** [***67-63-0***] was identified as a volatile metabolite in the ***breath*** . Specific, high organ-affinity was not obsd. in adult rats 24 h after single oral doses of [14C]PNU. However, the ureido C of PNU showed considerable retention in the blood, while relatively high residual levels were found in the ***liver*** for the Pr C. Autoradiog. studies on pregnant rats showed uniform distribution between maternal and fetal bodies a short time after dosing. A relatively high concn. of 14C was found in the maternal blood after 24 h with PNU (carbonyl-14C). Localization of the radioactivity in bone systems, such as fetal sterna and vertebrae, was noticed after 6 h with PNU (propyl-1-14C). Metabolic pathways of PNU are proposed and biochem. aspects of PNU metab. in rats are discussed.
ST propylnitrosourea metab; pregnancy nitrosourea propyl metab; placenta permeability propylnitrosourea
IT Air, respiratory
(***isopropanol*** of, after propylnitrosourea administration)
IT Placenta
(permeability of, to propylnitrosourea)
IT Pregnancy
(propylnitrosourea metab. during)
IT Urine
(propylnitrosourea metabolites of)
IT ***67-63-0*** , biological studies
RL: BIOL (Biological study)
(as propylnitrosourea metabolite, in ***breath***)
IT 57-13-6, biological studies 627-06-5
RL: BIOL (Biological study)
(as propylnitrosourea metabolite, in urine)
IT 816-57-9
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metab. of)

L12 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
AN 1978:437486 HCAPLUS

DN 89:37486
ED Entered STN: 12 May 1984
TI Effect of agents known to alter carbon tetrachloride ***hepatotoxicity* and cytochrome P-450 levels on carbon tetrachloride-stimulated lipid peroxidation and ethane ***expiration*** in the intact rat**
AU Lindstrom, Terry D.; Anders, M. W.
CS Dep. Pharmacol., Univ. Minnesota, Minneapolis, MN, USA
SO Biochemical Pharmacology (1978), 27(4), 563-7
CODEN: BCPCA6; ISSN: 0006-2952
DT Journal
LA English
CC 4-3 (Toxicology)
Section cross-reference(s): 1
AB Administration of CCl4 [56-23-5] (1 mL as 50% vol. soln., i.p.) to rats led to an increase in expired ethane [74-84-0] within 15 min. Prior treatment with phenobarbital Na [57-30-7] (50 mg/kg/day for 4 days, i.p.) increased CCl4-stimulated ethane ***expiration*** and ***hepatic*** microsomal lipid diene conjugation, whereas prior treatment with 3-methylcholanthrene [56-49-5] (20 mg/kg/day for 4 days, i.p.) or CCl4 led to a decrease in both parameters. Treatment with ***isopropanol*** [***67-63-0***] increased CCl4-stimulated ethane ***expiration*** , but EtOH [64-17-5] and diethyl maleate [141-05-9] treatment did not alter the response to CCl4. CoCl2 (60 mg/kg twice, s.c.) decreased CCl4-stimulated ethane ***expiration*** . A strong correlation was found between CCl4-stimulated ***hepatic*** microsomal lipid diene conjugation and ethane ***expiration*** . Cytochrome P450 may be involved in the formation of reactive intermediates responsible for CCl4-induced lipid peroxidn.
ST lipid peroxidn carbon tetrachloride drug; ethane ***expiration*** lipid peroxidn
IT ***Liver*** , metabolism
(lipid peroxidn. by, carbon tetrachloride effect on, ***liver*** microsomal enzyme inducers effect on)
IT Peroxidation
(of lipids, by ***liver*** , carbon tetrachloride effect on, ethane ***expiration*** in relation to)
IT Lipids
RL: BIOL (Biological study)
(peroxidn. of, by ***liver*** , carbon tetrachloride effect on, ***liver*** microsomal enzyme inducers effect on)
IT 56-49-5 57-30-7 64-17-5, biological studies ***67-63-0*** , biological studies 141-05-9 7646-79-9, biological studies
RL: BIOL (Biological study)
(carbon tetrachloride-stimulated ethane ***expiration*** and ***liver*** lipid peroxidn. response to)
IT 74-84-0, biological studies
RL: BIOL (Biological study)
(carbon tetrachloride-stimulated ***expiration*** of, ***liver*** microsomal enzyme inducers effect on, lipid peroxidn. in relation to)
IT 56-23-5, biological studies
RL: BIOL (Biological study)
(ethane ***expiration*** and lipid peroxidn. response to, ***liver*** microsomal enzyme inducers effect on)

L12 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1963:48965 HCAPLUS
DN 58:48965
OREF 58:8346d-g
ED Entered STN: 22 Apr 2001
TI Decomposition and toxicity of dialkylnitrosamines in rats
AU Heath, D. F.
CS Med. Res. Council Labs., Carshalton, UK
SO Biochemical Journal (1962), 85, 72-91
CODEN: BIJOAK; ISSN: 0264-6021
DT Journal
LA Unavailable
CC 69 (Toxicology, Air Pollution, and Industrial Hygiene)
AB To find out which compds. are responsible for the acute ***hepato**toxic*** action of dialkylnitrosamines, the metabolism in female rats of the following was studied: dimethyl-, diethyl-, butylmethyl-, and tert-butylmethylnitrosamine. Some of each nitrosamine was excreted unchanged in urine and expired in air. The dependence of rate on dose was detd. Rates of decompn. in vivo were detd. from the rate of ***expiration*** of C14O2 from rats given the compds. labeled in Me, Et, or Bu groups. The results agreed well when allowance was made for excretion and could be found with a coeff. of deviation of 6%. Labeled tert-butyl groups of tert-butylmethylnitrosamine, tert-butylamine or **2-methyl- ***2*** - ***propanol***** were not oxidized to C14O2. The rates of ***expiration*** of C14O2 showed that the decompn. of all but the tert-butyl compd. obeyed the Michaelis-Menten equation; and that the oxidn. of dimethylnitrosamine was inhibited competitively by the other 3 nitrosamines and by diethyl- and dimethylformamides. The ratio, Ki/Km for each of the inhibitors was as follows: dimethylformamide 2.79-2.31, dimethylnitrosamine 1.4-1.5, butylmethylnitrosamine 0.91-0.99, tert-butylmethylnitrosamine 2.3-2.7, bis(2-hydroxyethyl)nitrosamine 270, diethylformamide 1.54. The oxidn. of diethyl- and tert-butylmethylnitrosamines was also inhibited competitively by diethylformamide. Dimethylnitrosamine and dimethylformamide inhibited much the same range of sites. From their action it appeared that the other 3 nitrosamines were oxidized at at least 2 types of sites. The L.D.50 or E.D.50 (50% ***liver*** necrosis dose) values, or both, of the nitrosamines were detd.: dimethylnitrosamine L.D.50 34-6 mg./kg., E.D.50 19-22; butylmethylnitrosamine E.D.50 67-8. The tert-butyl compd. was without measurable necrotic activity. The E.D.50 values were unchanged by inhibitors that greatly increased the persistence of the nitrosamines in vivo. The nitrosamines themselves were not toxic, thus the toxic agent must be the product of oxidn. Most possible metabolites could not be postulated as the toxic agents unless drastic assumptions were made. The results were consistent with the assumption that the toxic agent in each case was a diazoalkane, or a monoalkylnitrosamine or carbonium ions formed from it.
IT 55-18-5, Diethylamine, N-nitroso- 62-75-9, Dimethylamine, N-nitroso- 2504-18-9, Ethylamine, N,1,1-trimethyl-N-nitroso- 7068-83-9, Butylamine, N-methyl-N-nitroso-
(metabolism and toxicity of)

L12 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1954:4272 HCAPLUS
DN 48:4272
OREF 48:824f-h

ED Entered STN: 22 Apr 2001
TI Feeding experiment on young calves with flaxseed residues which split off hydrogen ***cyanide***
AU Orth, A.; Mohr, F.
CS Landwirtschaft. Hochschule, Hohenheim, Germany
SO Archiv fuer Tierernaehrung (1953), 3, 31-9
CODEN: ARTIA2; ISSN: 0003-942X
DT Journal
LA Unavailable
CC 11E (Biological Chemistry: Nutrition)
AB The danger involved in the splitting of the flaxseed glycoride into HCN, grape sugar, and acetone was studied in young calves. Although HCN is an extremely toxic material, flaxseed and flaxseed products such as flaxseed cakes and extn. residues are used as nutrient materials in animal nutrition. Four kg./day of flaxseed cakes, and extn. salvage were fed to cattle in doses which theoretically exceeded the lethal dose of HCN with no toxic effects other than retarded appetites. A basic difference was demonstrated between animals with a simple digestive tract and those animals with a thick forestomach. In the former the activity of the flaxseed enzymes is destroyed by the gastric acidity, preventing the breakdown of the glycoside, whereas in ruminants the HCN is split off in 6-8 hrs., quickly resorbed from the mucus of the forestomach and taken care of through detoxification by the ***liver*** and ***expiration***. No evidence of accumulation of the HCN has been presented.
IT Flaxseed
(feeding expts. on calves with)
IT Feeding experiments
(with flaxseed on calves)
IT 74-90-8, Hydrocyanic acid
(from flaxseed glucoside, effect on calves)

L12 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1951:50687 HCAPLUS
DN 45:50687
OREF 45:8650d-g
ED Entered STN: 22 Apr 2001
TI Metabolism and toxicity of ***cyanides* and cyanogenetic glucosides in sheep. II. Detoxication of hydrogen ***cyanide*****
AU Blakley, R. L.; Coop, I. E.
CS Univ. New Zealand, Wellington
SO New Zealand Journal of Science and Technology, Section A: Agricultural Research Section (1949), 31A, 1-16
CODEN: NZTAA7; ISSN: 0369-6952
DT Journal
LA Unavailable
CC 11H (Biological Chemistry: Pharmacology)
AB cf. C.A. 44, 9067b; following abstr. Evidence is presented to show that in many animals **CN-** is mainly converted to SCN- which appears in the urine. HCN does not react in the rumen of sheep unless S compds. have been given by mouth. Only very small amts. of administered KCN appear as HCN or CN- in the urine, ***breath*** , or saliva of sheep or humans. Blood concns. of CN- in sheep after dosing with KCN are low, receding from a max. at about 15 min. after dosing to zero after about 5 hrs. Serum SCN- reaches much higher concns. and does not return to normal until 24-48 hrs. after dosing. SCN- formation from cystine and HCN in presence of sheep ***liver*** exts. has been studied, and it is suggested that it may

proceed through intermediate formation of .alpha.-amino-.beta.-thiocyanopropionic acid. SCN- synthesis from HCN in presence of ***liver*** ext. occurs much more rapidly utilizing sulfide or thiosulfate in place of cystine. The presence of H2S in the rumen and its rapid adsorption suggest that it is probably the most important S donor. SCN- is excreted into the urine slowly over a period of several days. Recoveries of over 50% have been obtained indicating that SCN- formation is the most important though not necessarily the only mode of detoxication. No evidence is found for cyanhydrin formation by glucose with HCN in presence of serum or ***liver*** ext.

IT Glycosides or Glucosides
Glycosides or Glucosides
(cyanogenic, metabolism of, and toxicity in sheep)

IT ***Cyanides***
Cyanides
(metabolism and toxicity in sheep)

IT Metabolism, animal
Metabolism, animal
(of ***cyanides*** and cyanogenetic glycosides)

IT Detoxication
Detoxication
(of hydrogen ***cyanide***)

IT 74-90-8, Hydrocyanic acid
(poisoning by, of sheep, and detoxication therein)

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File   9:Business & Industry(R) Jul/1994-2005/Nov 09
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         (c) 2005 ESPICOM Bus.Intell.
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         (c) 2005 The Gale Group
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         (c) 2005 Reed Business Information Ltd.
File 370:Science 1996-1999/Jul W3
         (c) 1999 AAAS
File 141:Readers Guide 1983-2004/Dec
         (c) 2005 The HW Wilson Co
Set     Items   Description
S1          0   RN=57-12-5 OR RN=67-63-0
S2      51789   CYANIDE OR CARBON()NITRIDE()ION OR HYDROCYANIC()ACID OR IS-
             OCYANIDE OR NITRILE()ANION OR CN OR CN1
S3      20050   (ISOPROPYL OR ISO()PROPYL OR SEC()PROPYL)()ALCOHOL OR (ISO
             OR 2)()PROPANOL OR ISOPROPANOL OR DIMETHYLCARBINOL OR IPA
S4      83370   HEPATITIS OR CIRRHOSIS OR RIFT()VALLEY()FEVER
S5       4817   CHIARI? ?()SYNDROME OR HEPATIC()VEIN()THROMBOSIS OR HEPATO-
             CELLULAR(N)CARCINOMA? ? OR HEPATOMA OR PORTOSYSTEMIC()ENCEPHA-
             LOPATHY
S6      47811   HEPATIC OR LIVER(1N)(DISEASE? ? OR NECROSIS OR TUMOR? ? OR
             TUMOUR? ? OR CANCER? ? OR NEOPLASM? ?) OR HEPATOTOXICITY
S7     118425   LIVER
S8     105511   BREATH OR EXHALATION OR EXPIRATORY OR EXHALE? ? OR EXHALING
S9     106430   EXPIRATION
S10       310   S2:S3(S)S4:S7
S11         4   S10(S)S8:S9
S12         4   RD (unique items)

 12/9/1     (Item 1 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01862692     SUPPLIER NUMBER: 56175755    (THIS IS THE FULL TEXT)
UNEXPLAINED OSMOL GAP FOLLOWING LACQUER THINNER INGESTION.
Brubacher, JR; Pudek, M; Filiatrault, L
Journal of Toxicology: Clinical Toxicology, 37, 5, 654
August, 1999
PUBLICATION FORMAT: Magazine/Journal; Refereed   ISSN: 0731-3810
LANGUAGE: English  RECORD TYPE: Fulltext; Abstract  TARGET AUDIENCE:
  Professional
WORD COUNT:   14    LINE COUNT:  00004
AUTHOR ABSTRACT:   Background: The osmol gap is commonly used as a marker
for toxic alcohol poisoning. We recently treated a patient who ingested
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lacquer thinner. No toxic alcohol was detected but over an 8 hour period the osmol gap increased from 15 mmol/kg to 31 mmol/kg. Case Report: The patient presented after ingesting ~250 mL of lacquer thinner. He had a solvent odor to his **breath** and was drowsy with slurred speech and nystagmus. Vitals were normal. Ethanol, salicylates, and acetaminophen were not detected. Electrolytes and blood gases were normal. The anion gap was 4 mmol/L. The osmol gap was 15 mmol/kg. An ethanol infusion was started. Three hours later methanol, ethylene glycol, acetone, and **isopropanol** were reported as negative but the osmol gap (accounting for ethanol) had increased to 20.5 mmol/kg. Ethanol was continued and serum reanalyzed. At 9 hours the osmol gap had increased to 31 mmol/kg but no toxic alcohols were detected and the patient had regained his normal mental status. Ethanol was stopped and the patient was discharged to psychiatry. Laboratory Methods: Three serum samples were analyzed by gas chromatography with head space analysis. No toxic alcohol was detected but volatile substances later identified as methyl ethyl ketone, toluene and xylene were present. We were unable to quantify these substances but the toluene and xylene peaks increased with time. Conclusion: We have presented a patient with an elevated osmol gap following lacquer thinner ingestion. Methyl ethyl ketone, toluene and xylene appear to have contributed to the osmol gap and should be considered when confronted with an unexplained osmol gap. Ongoing absorption and inhibition of **hepatic** metabolism likely contributed to the observed increase in osmol gap.
TEXT:
Brubacher JR, Pudek M, Filiatrault L. Vancouver General Hospital, Vancouver, British Columbia, Canada

DESCRIPTORS: Solvent abuse--Case studies; Thinner (Paint mixing)--Toxicology

12/3,K/3 (Item 3 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01487220 SUPPLIER NUMBER: 15694750 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Lipid peroxidation in workers exposed to lead.
Jiun, Yiin Shuenn; Hsien, Lin
Archives of Environmental Health, v49, n4, p256(4)
July-August, 1994
PUBLICATION FORMAT: Magazine/Journal ISSN: 0003-9896 LANGUAGE: English
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional
WORD COUNT: 1806 LINE COUNT: 00159
... Humad S, Zarling EJ, Skosey JL. Lipid peroxidation in rheumatoid arthritis: measurement of pentane in **breath** samples by gas chromatography. Clin Res 1985; 33:919A. [5.] Nishigake I, Hagihara M, Tsunekawa...
...acute myocardial infarction. J Clin Pathol 1984; 36:712-15. [7.] Suematsu T, Abe H. **Liver** and serum lipid peroxide levels in patients with **liver diseases** . In: Yagi K, Ed. Lipid peroxides in medicine and biology. New York: Academic Press, 1982...
...vivo. Biochem Pharmacol 1979; 28:2051-55. [13.] Burk RF, Lane JM. Ethane production and **liver necrosis** in rats after administration of drugs and other chemicals. Toxicol Appl Pharmacol 1979; 50:467...
...Inc., 1986; pp 584-609. [19.] Wong SHY, Knight JA, Hopfer SM, Zaharria O, Leach CN Jr, Sunderman FW Jr. Lipoperoxides in plasma as measured by liquid-chromatographic separation of malondialdehyde...

12/3,K/4 (Item 4 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01412630 SUPPLIER NUMBER: 13432710 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Anion and osmolal gaps in a patient with alcoholism.
Reuler, James B.; Poorman, Jay
The Western Journal of Medicine, v158, n2, p191(4)
Feb, 1993
PUBLICATION FORMAT: Magazine/Journal ISSN: 0093-0415 LANGUAGE: English
RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 3474 LINE COUNT: 00298
... elevation of acetoacetate, another cause of an elevated acetone level, particularly in chronic alcoholism, is **isopropyl alcohol** ingestion. This is explained by the fact that **isopropyl alcohol** is metabolized in the **liver** directly to acetone, which is subsequently excreted in the lungs, leading to a typical acetone **breath** , or, in larger quantities, through the urine, producing ketonuria.[4]
Laboratory results six hours after...

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File 307:DOSE
         (c) 2001 Royal Society of Chemistry
File 336:RTECS 2005/Q3
         Portions (c) Copyright 2005, U.S. Government. Rights Res
File 337:CHEMTOX (R) Online 1998/Q3
         (c)2005 Atrion International Inc.
File 304:The Merck Index Online(SM) 200(c) 2005 Merck & Co. Inc.
         5/S2
Set     Items   Description
S1          8   RN=57-12-5 OR RN=67-63-0
S2        508   CYANIDE OR CARBON()NITRIDE()ION OR HYDROCYANIC()ACID OR IS-
              OCYANIDE OR NITRILE()ANION OR CN OR CN1
S3       1619   (ISOPROPYL OR ISO()PROPYL OR SEC()PROPYL)()ALCOHOL OR (ISO
              OR 2)()PROPANOL OR ISOPROPANOL OR DIMETHYLCARBINOL OR IPA
S4        683   HEPATITIS OR CIRRHOSIS OR RIFT()VALLEY()FEVER
S5        131   CHIARI? ?()SYNDROME OR HEPATIC()VEIN()THROMBOSIS OR HEPATO-
              CELLULAR(N)CARCINOMA? ? OR HEPATOMA OR PORTOSYSTEMIC()ENCEPHA-
              LOPATHY
S6       1876   HEPATIC OR LIVER(1N)(DISEASE? ? OR NECROSIS OR TUMOR? ? OR
              TUMOUR? ? OR CANCER? ? OR NEOPLASM? ?) OR HEPATOTOXICITY
S7       7010   LIVER
S8        201   BREATH OR EXHALATION OR EXPIRATORY OR EXHALE? ? OR EXHALING
S9          2   EXPIRATION
S10         0   S1:S3(S)S4:S7(S)S8:S9
S11         5   S1:S3 AND S4:S7 AND S8:S9
S12       526   DIAGNOS?
S13         0   S11 AND S12
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FOREIGN AND INTERNATIONAL PATENTS

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File 350:Derwent WPIX 1963-2005/UD,UM &UP=200572
         (c) 2005  Thomson Derwent
File 347:JAPIO Nov 1976-2005/Jul(Updated 051102)
         (c) 2005 JPO & JAPIO
File 344:Chinese Patents Abs Aug 1985-2005/May
         (c) 2005 European Patent Office
Set     Items   Description
S1          0   RN=57-12-5 OR RN=67-63-0
S2     142031   CYANIDE OR CARBON()NITRIDE()ION OR HYDROCYANIC()ACID OR IS-
             OCYANIDE OR NITRILE()ANION OR CN OR CN1
S3      34697   (ISOPROPYL OR ISO()PROPYL OR SEC()PROPYL)()ALCOHOL OR (ISO
             OR 2)()PROPANOL OR ISOPROPANOL OR DIMETHYLCARBINOL OR IPA
S4      18206   HEPATITIS OR CIRRHOSIS OR RIFT()VALLEY()FEVER
S5       1155   CHIARI? ?()SYNDROME OR HEPATIC()VEIN()THROMBOSIS OR HEPATO-
             CELLULAR(N)CARCINOMA? ? OR HEPATOMA OR PORTOSYSTEMIC()ENCEPHA-
             LOPATHY
S6      12235   HEPATIC OR LIVER(1N)(DISEASE? ? OR NECROSIS OR TUMOR? ? OR
             TUMOUR? ? OR CANCER? ? OR NEOPLASM? ?) OR HEPATOTOXICITY
S7      28436   LIVER
S8      15297   BREATH OR EXHALATION OR EXPIRATORY OR EXHALE? ? OR EXHALING
S9       4380   EXPIRATION
S10      3961   S2:S3 AND S4:S7
S11         6   S10 AND S8:S9
S12     24688   BREATH?
S13         5   (S10 AND S12) NOT S11
```

11/26,TI/6 (Item 6 from file: 350)

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DIALOG(R)File 350:Derwent WPIX
(c) 2005  Thomson Derwent. All rts. reserv.
010465538
WPI Acc No: 1995-366857/199548
```

Tea for quickly dispelling the effects of alcohol

11/3,K/4 (Item 4 from file: 350)

```
DIALOG(R)File 350:Derwent WPIX
(c) 2005  Thomson Derwent. All rts. reserv.
011268115
WPI Acc No: 1997-246018/199723
XRAM Acc No: C97-079882
```

Preparation of medicine from chrysanthemum

```
Patent Assignee: HUANG G (HUAN-I)
Inventor: HUANG G
Number of Countries: 001  Number of Patents: 001
Patent Family:
Patent No     Kind   Date     Applicat No    Kind   Date     Week
CN 1100636     A   19950329  CN 93111748     A   19930921  199723  B
Priority Applications (No Type Date): CN 93111748 A 19930921
Patent Details:
Patent No  Kind Lan Pg   Main IPC     Filing Notes
CN 1100636    A        A61K-035/78
Abstract (Basic):  CN  1100636...
...clear summer damp-heat, improve sight and has a good effect on acute and
    chronic  hepatitis  and foul  breath .
```

11/3,K/5 (Item 5 from file: 350)

DIALOG(R)File 350:Derwent WPIX

011177932 **Image available**
WPI Acc No: 1997-155857/199715
XRAM Acc No: C97-050072

Combination of 5-lipoxygenase or leukotriene synthesis inhibitor - with glucocorticosteroids for treatment of inflammatory disease, esp. breathing disorders such as asthma

Patent Assignee: BAYER AG (FARB)
Inventor: BURCHARDT E; MULLER-PEDDINGHAUS R; MUELLER-PEDDINGHAUS R
Number of Countries: 045 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
DE 19532714	A1	19970306	DE 1032714	A	19950905	199715	B
WO 9709067	A1	19970313	WO 96EP3729	A	19960823	199717	
AU 9669844	A	19970327	AU 9669844	A	19960823	199729	

Priority Applications (No Type Date): DE 1032714 A 19950905
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
DE 19532714	A1		9	A61K-031/47	
WO 9709067	A1	G	27	A61K-045/06	

Designated States (National): AU BG BR BY CA CN CZ EE HU IS JP KE KP KR LT LV MX NO NZ PL RO RU SG SI SK UA US VN
Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE

AU 9669844 A A61K-045/06 Based on patent WO 9709067

...Abstract (Basic): LSI/LOI cpds. have formula (I). A, D, E, G, L, T = H, OH, halo, **CN** , COOH, NO2, CF3, OCF3, 1-8C alkyl, 1-8C alkoxy, 6-10C aryl (opt. substd. by halo, OH, NO2 or **CN**) (pref. H); R1 = H or 1-8C (pref. 1-6C) alkyl; R2 = H, OH or...

...respiratory conditions such as allergies -asthma, bronchitis, emphysema, shock lung, pulmonary hypertension-, and in the **liver** , kidney, intestines, pancreas, heart, nose, mouth, ears, eyes, musculature, CNS tissue, connective tissue; inflammation - rheumatism...

13/34/4 (Item 4 from file: 350)

DIALOG(R)File 350:Derwent WPIX

015893589 **Image available**
WPI Acc No: 2004-051424/200405

Self-diagnostic test for detecting mineral imbalance in user, contains mineral specific reagents each being selected to react with different selected mineral within biological sample

Patent Assignee: FUTURE DATA INC (FUTU-N); RUPP M E (RUPP-I)
Inventor: RUPP M E
Number of Countries: 103 Number of Patents: 007
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 20030203495	A1	20031030	US 2002375566	P	20020425	200405	B
			US 2003423130	A	20030424		
WO 200391725	A1	20031106	WO 2003US12911	A	20030425	200405	
AU 2003223735	A1	20031110	AU 2003223735	A	20030425	200442	
US 6821786	B2	20041123	US 2002375566	P	20020425	200477	
			US 2003423130	A	20030424		

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EP 1504257      A1  20050209  EP 2003719936   A   20030425  200512
                              WO 2003US12911  A   20030425
KR 2005020784   A   20050304  KR 2004717231   A   20041025  200548
JP 2005524071   W   20050811  WO 2003US12911  A   20030425  200554
                              JP 2004500061   A   20030425
Priority Applications (No Type Date): US 2002375566 P 20020425; US
  2003423130 A 20030424
Patent Details:
Patent No  Kind Lan Pg   Main IPC    Filing Notes
US 20030203495 A1    13 G01N-031/22   Provisional application US 2002375566
WO 200391725  A1 E     G01N-031/22
   Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA
   CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN
   IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ
   OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU
   ZA ZM ZW
   Designated States (Regional): AT BE BG CH CY CZ DE DK EA EE ES FI FR GB
   GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ
   UG ZM ZW
AU 2003223735 A1       G01N-031/22   Based on patent WO 200391725
US 6821786    B2       G01N-033/20   Provisional application US 2002375566
EP 1504257    A1 E     G01N-031/22   Based on patent WO 200391725
   Designated States (Regional): AL AT BE BG CH CY CZ DE DK EE ES FI FR GB
   GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
KR 2005020784 A        G01N-033/20
JP 2005524071 W     23 G01N-033/84   Based on patent WO 200391725
Abstract (Basic): US 20030203495 A1
        NOVELTY - Self-diagnostic test for detecting a mineral imbalance
    comprises mineral specific reagents each being selected to react with a
    different selected mineral within a biological sample such that when
    the selected mineral specific reagent is exposed to an adequate
    concentration of the selected mineral in the biological sample a
    visible change is induced in the selected mineral specific reagent.
        DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
        (a) a self-diagnostic test apparatus, comprising a body (10) having
    biological fluid receptacle(s); a biological sample conduit in fluid
    communication with the biological fluid receptacle; and the mineral
    specific reagents disposed such that each reagent may be exposed to a
    biological sample deposited within the biological fluid receptacle; and
        (b) a method of manufacturing the self-diagnostic test, comprising
    connecting the biological sample conduit with the biological fluid
    receptacle to provide a fluid connection in between; and depositing the
    mineral specific reagents within the body such that each reagent may be
    exposed to the biological sample deposited within the biological fluid
    receptacle.
        USE - For detecting a mineral imbalance in a user.
        ADVANTAGE - The inventive test is capable of accurately diagnosing
    an imbalance in an elemental mineral that can be both administered and
    analyzed at home by a patient. It is for those elements that do not
    occur naturally in the body. It is for those elements that are
    indicative of a specific disorder of the body, e.g. a combination
    copper/zinc analysis for Wilson's disease. It can be analyzed visually
    through calorimetric analysis. It is capable of measuring mineral
    imbalances in a patient's urine.
        DESCRIPTION OF DRAWING(S) - The figure is a schematic view of a
    diagnostic test.
        Body (10)
```

Reagent regions (12)
Indicator portion (14)
Scale (16)
pp; 13 DwgNo 2/4

Technology Focus:

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Component: The visual change is a colorimetric change. Each different substrate is a dipstick. A portion of the body is transparent such that the visible change of the selected mineral specific reagents may be externally viewed.

Preferred Method: The depositing step includes depositing each reagent independently within a different one of the biological fluid receptacles; or depositing each reagent on different substrate(s) removably disposed within the biological fluid receptacle.

BIOLOGY - Preferred Sample: The biological sample is blood, urine, saliva, mucous, tears, or hair.

ORGANIC CHEMISTRY - Preferred Component: The mineral specific reagents are selected to detect mineral(s) from a mineral family of microtrace, trace, mass, or all naturally occurring; or mineral(s) that does not occur naturally within a human body. They are selected to detect a mineral imbalance indicative of a disorder from attention deficit disorder (ADD)/attention deficit hyperactivity disorder (ADHD), Alzheimer's disease, anemia, ataxia, bipolar disorder, birth defects; blood disorders, brain damage, brain disease, breast cancer, **breathing** disorders, bone cancer, cardiomyopathy, general cancer, Crohn's disease, depressive disorders, encephalopathy, eye damage, heart damage, high blood pressure, infertility, intestinal disorders, leishmaniasis, **liver cancer** , **liver** damage, lung damage, lung disease, lung cancer, kidney damage, kidney disease, manic disorders, nerve damage, neuropathy, organ damage, pancreatic cancer, periodontal disease, psychosis, renal failure, skin disorders, or Wilson's disease; an imbalance in minerals from boron, germanium, iron, iodine, silicon, vanadium, chromium, cobalt, copper, nickel, molybdenum, scandium, zinc, tin, or manganese; an imbalance in minerals from calcium, chlorine, magnesium, phosphorus, sodium, or sulfur; an imbalance in minerals from lithium, beryllium, neon, aluminum, scandium, titanium, gallium, arsenic, bromine, krypton, rhodium, strontium, yttrium, zirconium, niobium, technetium, ruthenium, palladium, silver, cadmium, indium, antimony, tellurium, xenon, cesium, barium, lanthanum, hafnium, tantalum, tungsten, rhenium, osmium, iridium, platinum, gold, mercury, thallium, lead, bismuth, polonium, astatine, radon, francium, radium, actinium, cerium, praseodymium, neodymium, promethium, samarium, europium, gadolinium, terbium, dysprosium, holmium, erbium, ytterbium, lutetium, thorium, protactinium or uranium; or an imbalance in minerals from Neptunium, plutonium, americium, curium, berkelium, californium, einsteinium, fermium, mendelevium, nobelium, lanthanum, Rf (sic), Db (sic), Sg (sic), and Bh (sic). They are azomethine-H; chromotropic acid; dinitronaphthalenediol; 3,5-di-t-butylcatechol; 2,6-dihydroxybenzoic acid; curcumin; 5-hr-PAPS; o-nitrophenylfluorone; diphenylcarbazide; 5-Br-PADAP; BTAMB; TAMSMB; 5-Cl-PADAB; dithizone; 3,5-diBr-PAMB; nitroso-DMAP; nitroso-PSAP; nitroso-DEAP; 5-Br-PADAB; bathocuproin disulfonic acid disodium salt; bathocuproin; 3,5-diBr-PAESA; sodium bicinchoninate; neocuproin; 5-Br-PSAA; TMPyP; Na-DDTC; alfusone; chromazurol S; phenylfluorone; K2HGI4/I2; bindschedler's green leuco base; diphenylcarbazone: tris(1,10-phenanthroline)iron(II) complex; bathophenanthroline disulfonic acid disodium salt; TPTZ; PDTS; PDT; nitro-PAPS; PPKO;

ferrene S; PAR; oxine; DDTC; toluene-3,4-dithiol; PAN; dimethylglyoxime; bismuthiol-2; 2,3-diaminonaphthalene; PV; SATP; toluene-3,4-dithiol; henylfluorone 3,3-diaminobenzidine; o-phenylenediamine; 4 -chloro-o-phenylenediamine; ammonium molybdate; malachite green; BPA; zincon; XO; zinquin ethyl ester; or T(5-St)P. They are PC; MX; indo 1; indo 1-AM; chlorophosphonazo-III; neo-thorin; fluo 3; fluo 3-AM; arsenazo-III; HDOPP-Ca; rhod 2; rhod 2-AM; GHA; quin 2; quin 2-AM; calmagite; fura 2; fura 2-AM; thio-michler's ketone; MQAE; SPQ; diethylcarbamate-Cu; diphenylcarbazone; triocytlin; tris(1,10-phenanthroline)Fe(II); Co(3)-5-C1-PADAP; malachite green; bis(12-crown-4); nitrophenylazo-15-crown-5; oxine; pararosaniline; barium chloranilate; methylene blue; O-phthalaldehyde; p-phenylenediamine; tris(2-(phenyliminomethyl)pyridinato)iron; or 2-aminoperimidine hydrogen chloride/hydrogen bromide (HCl/HBr). They are lumogallion; o,o'-dihydroxyazobenzene; aluminon; oxine; 5-Br-PADAP; rhodamine B; brilliant green; arsemate; thionalide; nitrocatechol; ethyl violet; dimethylsulfonazo-III; sulfonazo-III; chlorophosphonazo-III; chromazural S; arsenazo-I; acetylacetone; beryllon-III; 2-methyloxine; bismuthio-II; XO; DDTC; dithizone; bindschedler's green leuco base; diphenylcarbazone; PAN; formaldoxime; pyrogallol red-AM; cesibor tetraphenylborate; europium actinide (EuAc3); europium oxide (Eu203); gadolinium actinide (GdAc3); gadolinium nitride (Gd(NO3)2); sincon; semiethylxylenol blue; potassium gold **dicyanide** (KAu(**CN**)2); sodium gold tetrachloride (NaAuC14); potassium gold tetrachloride (KAuC14); potassium gold tetraiodide (KAuI4); 5-(p-dimethylaminobenzylidene)rhodamine; PAR; potassium iridium chloride (K3IrCl6); sodium iridium chloride (Na3IrCl6); tin chloride (SnCl2)-HBr; leuco-crystal violet; lead actinide (PbAc2); lead chloride (PbC12); lead dinitride (Pb(NO3)2); methyl lead actinide (MePbAc); TPPS; thorin; bibenzyl-14-crown-4; phosphododecyl-14-crown-4; TTD-14-crown-4; methyldodecyl-12-crown-4; dibenzothiazolylmethane; ethyl mercury chloride (EtHgCl2); ethyl mercury phosphate (EtHgphosphate); mercury **dicyanide** (Hg(**CN**)2); ethyl mercury thiosalicylate (EtHgthiosalicylate, thiomersal); mersalyl; PCMB; PHMB; PCMBS; PhHgAc; mercury (II) chloride (HgCl2); mercury actinide (HgAc2); sulfuric acid; mercurochrome; Baker's reagent (2Hg); tetrakismercuryacetate (TAM)(4Hg); STTA; thio-Michler's ketone; di-alpha-napthaylthiocarbonate; sulfochlorophenol-S; TPAC; BPR; phenylfluorone; Os(NH3)6I3; potassium osmium chloride (K2OsCl6); potassium osmium oxide (K2OsO4); tiron; dipotassium palladium chloride K2PdCl4; dipotassium palladium bromide (K2PdBr4); dipotassium palladium iodide (K2PdI4); palladium chloride (PdCl2); palladium dinitride (Pd(NO3)2); BTAMB; 5-Br-PSAA; 5-Br-PAPS; thiooxine; p-nitroso-N,N'-dimethylaniline; dipotassium platinum tetrachloride (K2PtCl4); dipotassium platinum hexachloride (K2PtCl6); dipotassium iodide (K2PtI6; K2Pt(NO2)4; Pt(NH3)2Cl2; Pt(ethylenediamine)Cl2; dipotassium platinum **tetracyanide** (K2Pt(**CN**)4); rhenium chloride (ReCl2); 2-furildioxime; dimethylglyoxime; methylene blue; kalibor; TPTZ; 1,10-phenanthroline; samarium actinide (SmAc3); samarium nitride (Sm(NO3)3); samarium tetrachloride (SmCl4); 5,7-dichloro-oxine; quinizarin; silver nitrate (AgNO3); potassium silver **cyanide** (KagCN2); 3,5-diBr-PADAP; 3,5-diBr-PAESA; 2-amino-6-methylthio-4-pyrimidine-carboxylic acid; PC; dinitrosulfonazo-III; murexide; bismuthiol-2; diethydithiocarbamate; malachite green; thorium nitrate (Th(NO3)4); arsenazo-III; morin; diantipyrylmethane; O,O'-dihydroxyazobenzene; crystal violet; alizarin; disodium tungstate (N2WO4); toluene-3,4-dithiol; UO2Ac2; K3UO2F5;

UO2(NO3)2; UO2SO4; terbium tetrachloride (TbCl4); ytterbium actinide (YbAc3); zirconium nitrate (Zr(NO3)4); PV; TAN; or alizarin red S.
Derwent Class: B04; B05; S03
International Patent Class (Main): G01N-031/22; G01N-033/20; G01N-033/84
International Patent Class (Additional): G01N-021/01; G01N-021/29; G01N-021/78; G01N-031/20; G01N-033/48; G01N-033/52

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File 349:PCT FULLTEXT 1979-2005/UB=20051103,UT=20051027
         (c) 2005 WIPO/Univentio
Set     Items   Description
S1      81542   CYANIDE OR CARBON()NITRIDE()ION OR HYDROCYANIC()ACID OR IS-
             OCYANIDE OR NITRILE()ANION OR CN OR CN1
S2      55622   (ISOPROPYL OR ISO()PROPYL OR SEC()PROPYL)()ALCOHOL OR (ISO
             OR 2)()PROPANOL OR ISOPROPANOL OR DIMETHYLCARBINOL OR IPA
S3      22295   HEPATITIS OR CIRRHOSIS OR RIFT()VALLEY()FEVER
S4       7162   CHIARI? ?()SYNDROME OR HEPATIC()VEIN()THROMBOSIS OR HEPATO-
             CELLULAR(N)CARCINOMA? ? OR HEPATOMA OR PORTOSYSTEMIC()ENCEPHA-
             LOPATHY
S5      20201   HEPATIC OR LIVER(1N)(DISEASE? ? OR NECROSIS OR TUMOR? ? OR
             TUMOUR? ? OR CANCER? ? OR NEOPLASM? ?) OR HEPATOTOXICITY
S6      47388   LIVER
S7       8206   BREATH OR EXHALATION OR EXPIRATORY OR EXHALE? ? OR EXHALING
S8     202508   EXPIRATION
S9          8   S1:S2(S)S3:S6(S)S7:S8
S10     19387   BREATH?
S11         6   (S1:S2(S)S3:S6(S)S10) NOT S9

 9/6/1
01009846    **Image available**
AN ENZYME-BASED SYSTEM AND SENSOR FOR MEASURING ACETONE
 Publication Year: 2003


 9/3,AB,K/3
DIALOG(R)File 349:PCT FULLTEXT
(c) 2005 WIPO/Univentio. All rts. reserv.
00749273
ASSESSMENT OF GASTRIC EMPTYING DISORDERS
EVALUATION DE TROUBLES DE VIDANGE GASTRIQUE
Patent Applicant/Assignee:
  MASSTRACE INC, 3-G Gill Street, Woburn, MA 01801, US, US (Residence), US
    (Nationality); (For all designated states except: US)
Patent Applicant/Inventor:
  AJAMI Alfred M, 89 Glen Road, Apt. #8, Brookline, MA 02445, US, US
    (Residence), US (Nationality), (Designated only for: US)
Legal Representative:
  HEINE Holliday C, Weingarten, Schurgin, Gagnebin & Hayes LLP, Ten Post
    Office Square, Boston, MA 02109, US
Patent and Priority Information (Country, Number, Date):
  Patent:               WO 200061197 A1 20001019 (WO 0061197)
  Application:          WO 2000US9477 20000410  (PCT/WO US0009477)
  Priority Application: US 99128516 19990409
Designated States:
(Protection type is "patent" unless otherwise stated - for applications
prior to 2004)
  AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB
  GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA
  MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA
  UG US UZ VN YU ZA ZW
  (EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
  (OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
  (AP) GH GM KE LS MW SD SL SZ TZ UG ZW
  (EA) AM AZ BY KG KZ MD RU TJ TM
Publication Language: English
```

Filing Language: English
Fulltext Word Count: 9270
English Abstract
Methods of measuring gastric emptying time comprising providing to a patient a meal comprising a **breath** test food additive substrate, wherein the substrate is a linear or cyclic acyl aminoacid peptidomimetic that includes a radioactive or non- radioactively labeled carbon atom; having the patient digest the meal so that the carbon labeled nutrients therein are absorbed in the small intestine and metabolized to labeled CO<sb>2; and, at periodic intervals, detecting the level of labeled CO<sb>2 in **breath** samples taken from the patient to determine the rate of gastric emptying are disclosed.
Fulltext Availability: Claims
Claim
... FIGURE 4: OTZ as solid phase emptying probe
OTZ **Breath** Test
... Time after meal ingestion (Minutes)
FIGURE 5: OTZ as liquid phase emptying probe
OTZ **Breath** Test...
... Control Gastroesophageal reflux (GERD)
Hepatitis + portal hypertension (CLD)
INTERNATIONAL SEARCH REPORT
... Y MAES, B. D. ET AL: "Combined 1-23 carbon glycine/carbon octanoic acid **breath** test to monitor gastric emptying rates of liquids and solids"
J. NUCL. MED. (1994), 35...Online! 1-23
ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL;
BRADEN B. ET AL: "The '13C!acetate **breath** test accurately reflects gastric emptying of liquids in both liquid and semisolid test meals."...

9/3,AB,K/5
DIALOG(R)File 349:PCT FULLTEXT
(c) 2005 WIPO/Univentio. All rts. reserv.
00549622
VOLATILE BIOMARKERS FOR ANALYSIS OF HEPATIC DISORDERS
BIOMARQUEURS VOLATILS DESTINES A L'ANALYSE DE TROUBLES HEPATIQUES
Patent Applicant/Assignee:
THE JOHNS HOPKINS UNIVERSITY,
Inventor(s):
RISBY Terence H,
SEHNERT Shelley,
JIANG Long,
BURDICK James F,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200012995 A1 20000309 (WO 0012995)
Application: WO 99US19552 19990827 (PCT/WO US9919552)
Priority Application: US 9898467 19980831
Designated States:
(Protection type is "patent" unless otherwise stated - for applications prior to 2004)
AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK

MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU
ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH
CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW
ML MR NE SN TD TG

Publication Language: English
Fulltext Word Count: 17047
English Abstract

The present invention features test systems and methods for detecting a **hepatic** disorder in a mammal. The test systems and methods are designed especially for use with a primate. Preferred use of the invention involves staging the **hepatic** disorder in a human patient. In the test systems and methods, **respiratory gas constituents are monitored to detect and/or determine the state of the disorder.**

Fulltext Availability: Claims

Claim

... **LIVER DISEASE** STATUS
FIGR 4
15000
El HEPATOCELL
cn
w
I **cn**
j 10000
q
C
--I
m DIMETHYL SULFIDE
cn
=C a
m (pmol/L)
m a
I
:)o 5000- T
r@
r@
m
a
a
0.
I I
NONE EARLY MID
LIVER DISEASE STATUS
FiGn 5
800
HEPATOCELLULAR
C/y b
C: 600
m ETHANE
cn 400
(pmol/L)
m
C=
r@ 200
m a a
0 @ / 11A
I
NONE EARLY MID

LIVER DISEASE STATUS
FIGn 6
METHIONINE DEGRADATION
TRHOUGH THE TRANSAMINATIVE
PATHWAY IN **LIVER** MITOCHONDRIA
L-METHIONINE
2-OXO-1 -METHYL
THIOBUTYRIC ACID
co
cn
3-METHYLTHIO
PROPIONYL-CoA
m
cn
m
3-METHYLTHIO
PROPIONYL-CoA
HYDROGEN SULFIDE
rn
@071 [MALONYLSEMI- METHANETHIOL FORMALDEHYDE FOF
ALDEHYDE-CoA] 30
DIMETHYLSULFIDE SULFIDE SI
DIMETHYLDISULFIDE
OXIDATION OF SULFUR-CONTAING COMPOUND@
IN **LIVER** AND/OR ERYTHOCYTES
FiGn 7
INTERNATIONAL SEARCH REPORT International. application No.
PCT/US99/19552
A...
...practicable, search terms used) STN search in CA, MEDLINE, and BIOSIS
files using search terms: **liver** , **hepatic** , **disease** , disorder, marker,
biornarker, chromatog?, **breath** , gc
C. DOCUMENTS CONSIDERED TO BE RELEVANT
Category* Citation of document, with indication, where appropriate...
...HOTZ et al, "Development of a Method to Monitor Low Molecular 1
--- Mass Hydrocarbons in **Exhaled** **Breath** of Man: Preliminary ---Y
Evaluation of its Interest for Detecting a Lipoperoxidation Process...
...1987, Vol. 162, pages 303-310, see entire document.
X LETTERON et al, "Increased Ethane **Exhalation** , as an In Vivo 1
Index of Lipid Peroxidation, in Alcohol-Abusers" Gut, 1993, Vol...
...et al, "Evidence for Free Radical-Mediated Lipid I
--- Peroxidation at Reperfusion of Human Orthotopic **Liver** Transplants"
Y Surgery, 1994, Vol. 115, No. 1, pages 94-101, see entire document. 2...
...al, "Tunable Diode Laser Spectroscopy for Isotope Analysis I
-- Detection of Isotopic Carbon Monoxide in **Exhaled** **Breath** " ....

INVENTORS

```
File 350:Derwent WPIX 1963-2005/UD,UM &UP=200571
         (c) 2005  Thomson Derwent
File 349:PCT FULLTEXT 1979-2005/UB=20051103,UT=20051027
         (c) 2005 WIPO/Univentio
File 348:EUROPEAN PATENTS 1978-2005/Oct W04
         (c) 2005 European Patent Office
Set     Items   Description
S1       1035   AU='ISHIKAWA K' OR AU='ISHIKAWA K BIOL & CHEM RESLAB NISSAN
             CHEM INDC':AU='ISHIKAWA K NISSAN CHEM IND LTD SEIBUTSUKAGAKU'
S2          5   AU='ISHIKAWA KOUICHI'
S3        866   AU='ISHII Y' OR AU='ISHII Y KANSAI CNTR NAT INST ADV IND SC
              &TECH'
S4          4   AU='ISHII YUKIMOTO'
S5        204   AU='ASAI S' OR AU='ASAI S MITSUBISHI DENKI KABUSHIKI KAISH-
             A' OR AU='ASAI S T'
S6         14   AU='ASAI SATOSHI' OR AU='ASAI SATOSHI C O SHIN ETSU CHEMIC-
             AL CO LTD' OR AU='ASAI SATOSHI NIHON UNIVERSITY SCHOOL OF MED-
             ICI' OR AU='ASAI SATOSHI SILICONE ELECTRONICS MAT RES CTR'
S7        705   AU='NAKANO K' OR AU='NAKANO K CHUGAI SIYAKU KABUSHIKI KAIS-
             HA':AU='NAKANO K T'
S8         16   AU='NAKANO KAZUO' OR AU='NAKANO KAZUO C O OKI ELECTRIC IND-
             USTRY CO LTD':AU='NAKANO KAZUO RISO KAGAKU CORP R&D CENTER'
S9         31   AU='HASUMI K'
S10         6   AU='HASUMI KEIJI' OR AU='HASUMI KEIJI HITACHI TOKYO ELECTR-
             ONICS CO LTD'
S11     95835   LIVER OR HEPATIC
S12     50821   CIRRHOSIS OR PBC OR HEPATITIS OR STEATOHEPATITIS OR NASH OR
             BUDD()CHIARA OR HEPATOCELLULAR()CARCINOMA
S13    238102   CYANIDE OR ISOPROPANOL OR ISOPROPYL
S14     19442   BREATH
S15      2865   S1:S10
S16        16   S15 AND S11
S17         8   S15 AND S12
S18        43   S15 AND S13
S19         5   S15 AND S14
S20         3   S16:S17 AND S18
S21         2   S16:S17 AND S19
S22       662   S11:S12 AND S13 AND S14
S23         1   S15 AND S22
S24         3   S20:S21 NOT S23
S25         3   S18 AND (S11 OR S12 OR S14)
S26         0   S25 NOT (S20 OR S21 OR S23)
S27         3   S1:S10 AND S11:S12 AND S13
S28         0   S27 NOT (S20:S21 OR S23)

23/7/1     (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005  Thomson Derwent. All rts. reserv.
013806410    **Image available**
WPI Acc No: 2001-290622/200130
  A method and device for examining liver diseases such as hepatic
  cirrhosis comprises using an expiration analysis device for quantifying
  isopropanol and cyanide compounds
Patent Assignee: HITACHI TOKYO ELECTRONICS CO (HITN  ); UNIV NIPPON
  (UYNI-N)
```

Inventor: **ASAI S** ; **HASUMI K** ; **ISHII Y** ; **IS**HIKAWA K ; **NAKANO K**
Number of Countries: 094 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200125785	A1	20010412	WO 2000JP6979	A	20001006	200130 B
JP 2001108673	A	20010420	JP 99286335	A	19991007	200139
AU 200075578	A	20010510	AU 200075578	A	20001006	200143

Priority Applications (No Type Date): JP 99286335 A 19991007
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200125785	A1	J	22	G01N-033/497	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

JP 2001108673	A		8	G01N-033/497	
AU 200075578	A			G01N-033/497	Based on patent WO 200125785

Abstract (Basic): WO 200125785 A1

NOVELTY - A method for examining **liver** diseases comprises collection of expiration, quantifying **isopropanol** and/or **cyanide** compounds in the expiration, and analyzing the results.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a device for examining **liver** diseases using an expiration analysis device comprising an expiration analysis unit for introducing expiration to be analyzed, an analysis unit for quantifying **iso**propanol and/or **cyanide** compounds in the expiration, and a data processing unit for analyzing the analysis results sent from the expiration analysis unit.

USE - The method and device for examining **liver** diseases including chronic and acute **hepatitis** , fatty **liver** and particularly **hepatic cirrhosis** (claimed). The method is particularly used for the diagnosis of **hepatic cirrhosis** (claimed).

ADVANTAGE - The method of the invention is simple, rapid, highly-accurate and painless, without needing any special operator.

DESCRIPTION OF DRAWING(S) - Simplified structure of an expiration analysis device is shown. (Drawing includes non-English language text).

Expiration analysis device (1A)
mouth piece (2)
expiration-switching valves (3, 4)
valve body (5)
expiration-trapping bag (6)
flow controller (7)
heater (8)
mixed gas (9)
expiration collection unit (28)
expiration analysis unit (29)
data processing unit (30)
pp; 22 DwgNo 1/5

Derwent Class: B04; S03
International Patent Class (Main): G01N-033/497
International Patent Class (Additional): A61B-010/00; G01N-001/00; G01N-001/02; G01N-027/62; G01N-030/88; G01N-033/98

```
File 155:MEDLINE(R) 1951-2005/Nov 07
         (c) format only 2005 Dialog
File   5:Biosis Previews(R) 1969-2005/Nov W1
         (c) 2005 BIOSIS
File  73:EMBASE 1974-2005/Nov 09
         (c) 2005 Elsevier Science B.V.
File  34:SciSearch(R) Cited Ref Sci 1990-2005/Oct W5
         (c) 2005 Inst for Sci Info
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
Set     Items   Description
S1       9372   AU=ISHIKAWA K?
S2       7531   AU=ISHII Y?
S3       1621   AU=ASAI S?
S4       5465   AU=NAKANO K?
S5        992   AU=HASUMI K?
S6    2251723   LIVER OR HEPATIC
S7     668519   CIRRHOSIS OR PBC OR HEPATITIS OR STEATOHEPATITIS OR NASH OR
              BUDD()CHIARA OR HEPATOCELLULAR()CARCINOMA
S8     109863   CYANIDE OR ISOPROPANOL OR ISOPROPYL
S9     218097   BREATH OR EXPIR?
S10         6   S1:S5 AND S6:S7 AND S8
S11         0   S9 AND S10
S12         3   RD S10 (unique items)
S13     77274   BREATH
S14      6906   S6:S7 AND S13
S15        62   S1:S5 AND S14
S16        62   S6:S7 AND S15
S17         0   S15 AND S8
S18        62   S6:S7(S)S15
S19   6096739   DIAGNOS?
S20        22   S18 AND S19
S21        19   RD (unique items)
S22        19   Sort S21/ALL/PY,A

12/7/2     (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2005 Dialog. All rts. reserv.
08955764   PMID: 2561216
  Increased iodine-123-iodoamphetamine uptake in hepatomas.
  Suto Y;  Ishii Y ; Caner B E; Noguchi M; Katsube Y; Torizuka K
  Department of Radiology, Tottori University, School of Medicine, Japan.
  Radiation medicine (JAPAN) Nov-Dec 1989, 7 (6) p274-7, ISSN
0288-2043  Journal Code: 8412264
  Publishing Model Print
  Document type: Case Reports; Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed
  In the current study, two cases of hepatoma are reported in which N-
isopropyl -(I-123)-p-iodoamphetamine (IMP) liver scan demonstrated
increased accumulation in the tumor corresponding to the areas enhanced on
contrast enhanced CT (CE-CT). In contrast, there was no IMP accumulation in
the necrotic area of the tumor in which no enhancement was found on CE-CT.
Thus, IMP liver scan seems to have the potential to assess the viability
of a hepatoma as well as to detect and localize it.
  Record Date Created: 19900524
```

Record Date Completed: 19900524

12/7/3 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

04894654 EMBASE No: 1992034869
Pharmacological properties of YM-21095, a potent and highly specific renin inhibitor
Shibasaki M.; Asano M.; Fukunaga Y.; Usui T.; Ichihara M.; Murakami Y.; **Nakano K.** ; Fujikura T.
Medicinal Research Laboratories II, Central Research Laboratories, Yamanouchi Pharmaceutical Co., Ltd., 21 Miyukigaoka, Tsukuba, Ibaraki 305 Japan
American Journal of Hypertension (AM. J. HYPERTENS.) (United States) 1991, 4/12 I (932-938)
CODEN: AJHYE ISSN: 0895-7061
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
A novel renin inhibitor, YM-21095 ((2RS), (3S)-3-(N(alpha)-(1,4-dioxo-4-morpholino-2-(1-naphthylmethyl)-buthyl)-L histidil-amino)-4-cyclohexyl-1-((1-methyl-5-tetrazolyl)thio)-2-butano l), has been synthesized in our laboratories. The aim of this study was to evaluate the pharmacological properties of YM-21095 in in vitro and in vivo experiments. YM-21095 inhibited human renin with an IC$D5inf 0 value of 4.7 x 10sup -sup 1sup 0 mol/L. YM-21095 was also a potent inhibitor against squirrel monkey renin, but less effective against renins from dog, rabbit, and rat. The effect of YM-21095 is highly specific for renin, since it did not inhibiti cathepsin D, pepsin, or angiotensin converting enzyme up to a concentration of 10sup -sup 4 mol/L. YM-21095 was resistant to proteolytic actions of the enzymes (pepsin, chymotrypsin, trypsin) and squirrel monkey tissue homogenates (**liver** , kidney, small intestine). Itravenous infusion of YM-21095 (0.1 to 100 mug/kg/min) decreased mean blood pressure and inhibit plasma renin activity in a dose-dependent manner with no effect on heart rate in anesthetized sodium-depleted and sodium-replete squirrel monkeys. The hypotensive effect of YM-21095 in sodium-depleted squirrel monkeys was about ten times as potent as that in sodium-replete squirrel monkeys. Oral administration of YM-21095 to conscious sodium-depleted squirrel monkeys produced dose-related decreases of systolic blood pressure. We conclude that YM-21095 is a potent and highly specific inhibitor of primate renin and produces a blood pressure lowering effect.

22/9/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13487378 PMID: 10452879
13CO(2) peak value of L-[1-(13)C]phenylalanine breath test reflects hepatopathy.
Ishii Y; Asai S; Kohno T; Suzuki S; Ishii M; Hosoi I; Fujii M; Iwai S; **Ishikawa K**
Department of Pharmacology, 3rd Department of Surgery, Nihon University School of Medicine, Itabashi-ku, Tokyo, 173, Japan.
Journal of surgical research (UNITED STATES) Sep 1999, 86 (1) p130-5 , ISSN 0022-4804 Journal Code: 0376340
Publishing Model Print
Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

BACKGROUND: Using a rat model of hepatectomy, we investigated whether the severity of hepatopathy could be quantitatively measured from changes in expiratory (13)CO(2) levels after intravenous administration of L-[1-(13)C]methionine or L-[1-(13)C]phenylalanine. MATERIALS AND METHODS: Under nembutal anesthesia, 30 mg/kg L-[1-(13)C]phenylalanine or 40 mg/kg L-[1-(13)C]methionine was administered to rats through the femoral vein, and expiratory (13)CO(2) levels were measured for 15 min. A 30, 70, or 90% hepatectomy was performed. In the control group, simple laparotomy was performed. **Breath** test was conducted 20 min after laparotomy. We examined the correlation of the total (13)CO(2) output over 15 min or peak (13)CO(2) level with **liver** weight/body weight (%). RESULTS: In **breath** test graphs, L-[1-(13)C]methionine did not show any peak level during measurement. L-[1-(13)C]phenylalanine showed a specific peak level 6 +/- 1 min after administration. The correlation coefficient between total (13)CO(2) output over 15 min after L-[1-(13)C]methionine administration and **liver** weight/body weight was 0.922 ($P < 0.001$). The correlation coefficient between total (13)CO(2) output over 15 min after L-[1-(13)C]phenylalanine administration and **liver** weight/body weight was 0.883 ($P < 0.001$). The correlation coefficient between peak L-[1-(13)C]phenylalanine level and **liver** weight/body weight was highest, 0.927 ($P < 0.001$). CONCLUSION: In a **breath** test with intravenously administered L-[1-(13)C]methionine or L-[1-(13)C]phenylalanine, hepatopathy could be quantitatively evaluated by measuring expiratory (13)CO(2) levels over 15 min. After administration of L-[1-(13)C]phenylalanine, hepatopathy could be quantitatively evaluated in a short period by measuring the peak expiratory (13)CO(2) level. Copyright 1999 Academic Press.

Tags: Male; Research Support, Non-U.S. Gov't

Descriptors: *Breath Tests; * **Liver** Diseases-- **diagnosis** --DI; *Phenylalanine-- **diagnostic** use--DU; *Respiration; Animals; Body Weight; Carbon Dioxide; Carbon Isotopes; Hepatectomy--methods--MT; **Liver** --pathology--PA; Organ Size; Rats; Rats, Wistar

CAS Registry No.: 0 (Carbon Isotopes); 124-38-9 (Carbon Dioxide); 63-91-2 (Phenylalanine)

Record Date Created: 19990923
Record Date Completed: 19990923

22/9/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0012072001 BIOSIS NO.: 199900331661
Determination of liver **regeneration rate in partially-hepatectomized rats by the L-(1-C)phenylalanine** breath **test**
AUTHOR: **Ishii Yukimoto** (Reprint); Kohno T; **Asai S**; Suzuki S; Kato K; Fujii M; **Ishikawa K**; Iwai S
AUTHOR ADDRESS: Nihon Univ Sch of Medicine, Tokyo, Japan**Japan
JOURNAL: Gastroenterology 116 (4 PART 2): pA1223 April, 1999 1999
MEDIUM: print
CONFERENCE/MEETING: Digestive Disease Week and the 100th Annual Meeting of the American Gastroenterological Association Orlando, Florida, USA May 16-19, 1999; 19990516
SPONSOR: American Gastroenterological Association
ISSN: 0016-5085

DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 63-91-2Q: phenylalanine; 150-30-1Q: phenylalanine
DESCRIPTORS:
MAJOR CONCEPTS: Gastroenterology--Human Medicine, Medical Sciences; Methods and Techniques
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae); rat (Muridae)
ORGANISMS: PARTS ETC: **liver** --digestive system
COMMON TAXONOMIC TERMS: Humans; Primates; Animals; Chordates; Mammals; Nonhuman Vertebrates; Nonhuman Mammals; Rodents; Vertebrates
CHEMICALS & BIOCHEMICALS: phenylalanine--metabolism
METHODS & EQUIPMENT: hepatectomy--partial, surgical method; L-{1-C}-phenylalanine breath test-- **diagnostic** method
MISCELLANEOUS TERMS: **liver** regeneration rate; Meeting Abstract; Meeting Abstract
CONCEPT CODES:
14001 Digestive system - General and methods
11107 Anatomy and Histology - Regeneration and transplantation
12504 Pathology - Diagnostic
16001 Respiratory system - General and methods
22002 Pharmacology - General
13002 Metabolism - General metabolism and metabolic pathways
00520 General biology - Symposia, transactions and proceedings
BIOSYSTEMATIC CODES:
86215 Hominidae
86375 Muridae

22/9/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2005 Dialog. All rts. reserv.
13059457 PMID: 11025368
[1-(13)C]Galactose breath test for quantitative measurement of liver function in a short period.
Suzuki S; **Ishii Y**; **Asai S**; Kohno T; Mazaki T; Takahashi Y; Iwai S; **Ishikawa K**
Department of Pharmacology, Nihon University School of Medicine, Tokyo, Japan.
Digestion (SWITZERLAND) 2000, 62 (2-3) p194-9, ISSN 0012-2823
Journal Code: 0150472
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS
BACKGROUND: Using a rat model of hepatectomy, we investigated whether the severity of hepatopathy could be quantitatively measured from changes in expiratory (13)CO(2) levels after intravenous administration of [1-(13)C]galactose. MATERIALS ANd METHODS: Under nembutal anesthesia, 100 mg/kg [1-(13)C]galactose was administered to rats via the femoral vein, and expiratory (13)CO(2) levels were measured for 60 min. Then, 30, 70 or 90% hepatectomy was performed. In the control group, simple laparotomy was performed. **Breath** test was conducted 20 min after laparotomy. We examined

the correlation of total (13)CO(2) output (S) or single point (13)CO(2) level (SP) every 5 min until 30 min, and at 45 and 60 min with **liver** weight/body weight (LW/BW) (%). RESULTS: In the control group, the **breath** test graph reached a plateau level, but in all groups undergoing hepatectomy a plateau level was not reached during measurement. The correlation coefficient between S(30) after [1-(13)C]galactose administration and LW/BW was 0.889 ($p< 0.0001$). The correlation coefficient between SP(25) after [1-(13)C]galactose administration and LW/BW was highest, 0.923 ($p< 0.0001$). CONCLUSION: In the **breath** test with intravenously administered [1-(13)C]galactose, hepatopathy could be evaluated by measuring S(30) and hepatopathy could be more accurately quantitatively evaluated by measuring SP(25) over a short period. Copyright 2000 S. Karger AG, Basel.

Tags: Male; Research Support, Non-U.S. Gov't

Descriptors: *Galactose--metabolism--ME; *Hepatectomy; * **Liver** Diseases -- **diagnosis** --DI; Animals; Breath Tests; Carbon Dioxide--analysis--AN; Carbon Isotopes-- **diagnostic** use--DU; Disease Models, Animal; Infusions, Intravenous; **Liver** Function Tests--veterinary--VE; Rats; Rats, Wistar; Sensitivity and Specificity

CAS Registry No.: 0 (Carbon Isotopes); 124-38-9 (Carbon Dioxide); 26566-61-0 (Galactose)

Record Date Created: 20001113

Record Date Completed: 20010111

22/9/5 (Item 5 from file: 73)

DIALOG(R)File 73:EMBASE

11735883 EMBASE No: 2002309951

Evaluation of liver **regeneration using the L-[1-SUP13C]methionine** breath **test**

Ishii Y.; **Asai S.**; Kohno T.; Takahashi Y.; Nagata T.; Suzuki S.; Kohno T.; Iwai S.; **Ishikawa K.**

Dr. Y. Ishii, Department of Pharmacology, Nihon University School of Medicine, Oyaguchi-Kami Machi, Itabashi, Tokyo 173 Japan

AUTHOR EMAIL: yishii@med.nihon-u.ac.jp

Journal of Surgical Research (J. SURG. RES.) (United States) 2001, 95/2 (195-199)

CODEN: JSGRA ISSN: 0022-4804

DOCUMENT TYPE: Journal ; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 18

Background. We examined the relationship between changes in the **liver** weight/body weight percentage, amount of **hepatic** tissue total DNA, and the results of the [1-SUP13C]methionine (SUP13Cmet) **breath** test during **hepatic** regeneration in a rat model of 70% hepatectomy, to assess their usefulness for evaluating **hepatic** regeneration. Materials and methods. Male Wistar rats (230-290 g) were subjected to 70% hepatectomy under anesthesia with Nembutal. One, 2, 3, 7, and 14 days postoperatively, 40 mg/kg SUP13Cmet was intravenously injected into the femoral vein, and the increase in exhaled SUP13COSUB2 (DELTASUP13COSUB2) was measured for 15 min. Simple laparotomy was performed in control rats. Following the **breath** test, the regenerated **liver** was removed and weighed. The amount of DNA was determined. Results. The correlation coefficients (r) between **liver** weight/body weight (LW/BW) and results of the SUP13Cmet **breath** test, and between DNA and results of the SUP13Cmet **breath** test were 0.892 and 0.800, respectively. Conclusions. The SUP13Cmet **breath** test is considered

to be very useful for assessing **liver** regeneration, and total SUP13COSUB2 output over 15 min in the SUP13Cmet **breath** test graph seems to be an effective indicator for evaluating **liver** regeneration. (c) 2001 Academic Press.
MANUFACTURER NAMES: Icon/United States
DRUG DESCRIPTORS:
*methionine derivative--intravaginal drug administration--va
DNA--endogenous compound--ec; pentobarbital; unclassified drug
MEDICAL DESCRIPTORS:
* **liver** regeneration; *breath analysis; * **liver** resection
liver weight; body weight; tissue level; evaluation; rat strain; anesthesia; postoperative period; femoral vein; expired air; laparotomy; DNA content; correlation coefficient; **diagnostic** value; nonhuman; male; rat; animal experiment; controlled study; animal tissue; article; priority journal
DRUG TERMS (UNCONTROLLED): methionine c 13--intravenous drug administration --iv
CAS REGISTRY NO.: 9007-49-2 (DNA); 57-33-0, 76-74-4 (pentobarbital)
SECTION HEADINGS:
009 Surgery
021 Developmental Biology and Teratology
037 Drug Literature Index
048 Gastroenterology

22/9/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0013477416 BIOSIS NO.: 200200070927
% 13C dose H-1 maximum value of (1-13C) phenylalanine breath test reflects phenylalanine hydroxylase activity
AUTHOR: **Ishii Yukimoto** (Reprint); Suzuki Shigeru (Reprint); Kohno Tomohisa (Reprint); Hara Jyunko (Reprint); Aoki Masaru (Reprint); **Asai Satoshi** (Reprint); Takayama Tadatoshi (Reprint)
AUTHOR ADDRESS: Nihon Univ School of Medicine, Itabashi City, Tokyo, Japan **Japan
JOURNAL: Hepatology 34 (4 Pt. 2): p692A October, 2001 2001
MEDIUM: print
CONFERENCE/MEETING: 52nd Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA November 09-13, 2001; 20011109
ISSN: 0270-9139
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 63-91-2Q: phenylalanine; 150-30-1Q: phenylalanine; 9029-73-6: phenylalanine hydroxylase
DESCRIPTORS:
MAJOR CONCEPTS: Digestive System--Ingestion and Assimilation; Enzymology --Biochemistry and Molecular Biophysics; Methods and Techniques
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)--patient
ORGANISMS: PARTS ETC: **liver** --digestive system
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: digestive disease--digestive system disease

CHEMICALS & BIOCHEMICALS: { 1-carbon-13}phenylalanine-- **diagnostic** -drug , oral administration; carbon dioxide-13}; phenylalanine--metabolism; phenylalanine hydroxylase{
METHODS & EQUIPMENT: 1-carbon-13}phenylalanine breath test-- **diagnostic** method
MISCELLANEOUS TERMS: percent {carbon-13}; Meeting Abstract; Meeting Abstract
CONCEPT CODES:
00520 General biology - Symposia, transactions and proceedings
10064 Biochemistry studies - Proteins, peptides and amino acids
10802 Enzymes - General and comparative studies: coenzymes
12504 Pathology - Diagnostic
13002 Metabolism - General metabolism and metabolic pathways
14004 Digestive system - Physiology and biochemistry
14006 Digestive system - Pathology
BIOSYSTEMATIC CODES:
86215 Hominidae

22/9/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14517335 PMID: 12464870

Recovery of liver function in two-third partial hepatectomized rats evaluated by L-[1-13C]phenylalanine breath test.

Ishii Yukimoto; Asai Satoshi; Kohno Tadashi; Ito Asuka; Iwai Shigetomi; **Ishikawa Koichi**
Departments of Pharmacology and Third Department of Surgery, Nihon University School of Medicine, Itabashi-ku, Tokyo, Japan.

Surgery (United States) Nov 2002, 132 (5) p849-56, ISSN 0039-6060
Journal Code: 0417347
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: AIM; INDEX MEDICUS

BACKGROUND: We have previously reported that by means of a **breath** test with intravenously administered L-[1-13C] phenylalanine (13Cphe), hepatopathy could be quantitatively evaluated by measuring expiratory 13CO2 levels in a short period. It is known that phenylalanine hydroxylase activity (PAHA) plays an important role in phenylalanine metabolism. We examined the relationship between changes in PAHA and the results of the 13Cphe **breath** test during **hepatic** regeneration in a rat model of 70% hepatectomy, to assess their usefulness for evaluating **hepatic** regeneration. METHODS: Male Wistar rats (Shizvoka Laboratory Animal Center, Hamamatsu, Japan) weighing 230 to 290 g were subjected to 70% hepatectomy under anesthesia with sodium pentobarbital. One, 2, 3, 5, 7, and 14 days postoperatively, 30 mg/kg 13Cphe was intravenously injected into the femoral vein, and the increase in exhaled 13CO2 (Delta 13CO2) was measured for 15 minutes. Simple laparotomy was performed in control rats. After the **breath** test, the regenerated **liver** was removed and weighed. The amount of DNA, amount of **hepatic** tissue total protein (TP), and PAHA were determined. RESULTS: The r between **liver** weight/body weight and PAHA, between DNA and PAHA, and between TP and PAHA were 0.832, 0.720, and 0.758, respectively. **Breath** test graphs revealed that **liver** weight/body weight, DNA, and TP showed the best correlations with the peak value of

Delta 13CO2 (**liver** weight/body weight percentage, r = 0.801; DNA, r = 0.660; TP, r = 0.706), and r between PAHA and peak value was 0.638. CONCLUSIONS: These results suggest that measurement of PAHA in regenerated **liver** is an effective method for following up **liver** function after **hepatic** resection. Moreover, the 13Cphe **breath** test may also be useful to evaluate **liver** function after partial hepatectomy.

Tags: Male; Research Support, Non-U.S. Gov't

Descriptors: *Breath Tests; *Hepatectomy--methods--MT; * **Liver** --physiopathology--PP; * **Liver** Function Tests; *Phenylalanine-- **diagnostic** use--DU; Animals; Body Weight; Carbon Isotopes-- **diagnostic** use--DU; DNA --metabolism--ME; **Liver** --metabolism--ME; **Liver** --pathology--PA; **Liver** Regeneration--physiology--PH; Organ Size; Phenylalanine Hydroxylase --metabolism--ME; Proteins--metabolism--ME; Rats; Rats, Wistar; Recovery of Function

CAS Registry No.: 0 (Carbon Isotopes); 0 (Proteins); 63-91-2 (Phenylalanine); 9007-49-2 (DNA)

Enzyme No.: EC 1.14.16.1 (Phenylalanine Hydroxylase)

Record Date Created: 20021204

Record Date Completed: 20030103

22/9/9 (Item 9 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

14360438 PMID: 12187622

[Evaluation of liver **function with 13C-labelled amino acid using hepatectomized rat model]**

Ishii Yukimoto; Ishikawa Koichi; Asai Satoshi

Department of Surgery Division 3, Nihon University School of Medicine, Itabashi-ku, Tokyo 173-8610, Japan. yishii@med.nihon-u.ac.jp

Nippon yakurigaku zasshi. Japanese journal of pharmacology (Japan) Aug 2002, 120 (2) p101-6, ISSN 0015-5691 Journal Code: 0420550

Publishing Model Print

Document type: Journal Article ; English Abstract

Languages: JAPANESE

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Using a rat model of hepatectomy, we investigated whether the severity of hepatopathy could be quantitatively measured from changes in expiratory 13CO2 levels after intravenous administration of L-[1-(13)C]phenylalanine, L-[1-(13)C]methionine or L-[1-(13)C]alanine. MATERIALS AND METHODS: Under nembutal anesthesia, 30 mg/kg L-[1-(13)C]phenylalanine, 40 mg/kg L-[1-(13)C]methionine or 20 mg/kg L-[1-(13)C]alanine was administered to rats through the femoral vein, and expiratory 13CO2 levels were measured for 15 min. Thirty percent, 70% or 90% hepatectomy was performed. In the control group, simple laparotomy was performed. RESULTS: The correlation coefficient between total 13CO2 output over 15 min after L-[1-(13)C]phenylalanine administration and **liver** weight/body weight was 0.883 ($P < 0.001$). The correlation coefficient between total 13CO2 output over 15 min after L-[1-(13)C]methionine administration and **liver** weight/body weight was 0.922 ($P < 0.001$). The correlation coefficient between total 13CO2 output over 15 min after L-[1-(13)C]alanine administration and **liver** weight/body weight was 0.902 ($P < 0.0001$). CONCLUSION: In the **breath** test with intravenously administered L-[1-(13)C]phenylalanine, L-[1-(13)C]methionine, or L-[1-(13)C]alanine, hepatopathy could be quantitatively evaluated by measuring expiratory 13CO2

levels over 15 min.
Descriptors: *Amino Acids-- **diagnostic** use--DU; *Breath Tests--methods --MT; *Carbon Dioxide--analysis--AN; * **Liver** Function Tests--methods--MT; Alanine-- **diagnostic** use--DU; Animals; Carbon Radioisotopes-- **diagnostic** use--DU; Hepatectomy; Methionine-- **diagnostic** use--DU; Phenylalanine-- **diagnostic** use--DU; Radiopharmaceuticals-- **diagnostic** use--DU; Rats
CAS Registry No.: 0 (Amino Acids); 0 (Carbon Radioisotopes); 0 (Radiopharmaceuticals); 124-38-9 (Carbon Dioxide); 56-41-7 (Alanine); 63-68-3 (Methionine); 63-91-2 (Phenylalanine)
Record Date Created: 20020821
Record Date Completed: 20021003

22/9/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2005 Dialog. All rts. reserv.
14084050 PMID: 11855912
1-[1-(13)C]Alanine is a useful substance for the evaluation of liver **function**
Suzuki Shigeru; **Ishii Yukimoto; Asai Satoshi**; Kohno Tadashi; Mazaki Takerou; Takahashi Yasuo; Kohno Tomohisa; **Ishikawa Koichi**
Department of Pharmacology, Third Department of Surgery, Nihon University School of Medicine, Itabashi-ku, Tokyo, 173, Japan.
Journal of surgical research (United States) Mar 2002, 103 (1) p13-8 , ISSN 0022-4804 Journal Code: 0376340
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS
BACKGROUND: Using a rat model of hepatectomy, we investigated whether the severity of hepatopathy could be quantitatively measured from changes in expiratory (13)CO(2) levels after intravenous administration of 1-[1-(13)C]alanine. MATERIALS AND METHODS: Under nembutal anesthesia, 20 mg/kg 1-[1-(13)C]alanine was administered to rats via the femoral vein, and expiratory (13)CO(2) levels were measured for 15 min. Then, 30, 70, or 90% hepatectomy was performed. In the control group, simple laparotomy was performed. A **breath** test was conducted 20 min after laparotomy. We examined the correlation of total (13)CO(2) output (S) or single point (13)CO(2) level (SP) every 1 min for 15 min with **liver** weight/body weight (LW/BW) (%). RESULTS: In the control group, the **breath** test graph showed a specific peak level about 3 min after administration, but in all groups undergoing hepatectomy, it did not show any peak level during measurement. The correlation coefficient between S(12--15) after 1-[1-(13)C]alanine administration and LW/BW was 0.902 ($P < 0.0001$). The correlation coefficient between SP(7) after 1-[1-(13)C]alanine administration and LW/BW was highest, 0.908 ($P < 0.0001$). The severity of hepatopathy could also be evaluated, with significant differences in S(12-14) compared to control when the volume of resected **liver** was 30% or greater, but there was no significant difference between the groups undergoing 70 and 90% hepatectomy. However, the severity of hepatopathy could be evaluated, with significant differences in S(15) and SP(7) in all comparisons between groups. CONCLUSION: In the **breath** test with intravenously administered 1-[1-(13)C]alanine, the severity of hepatopathy could be quantitatively evaluated in a short period by measuring S(15) and SP(7).
Tags: Male; Research Support, Non-U.S. Gov't
Descriptors: *Alanine--pharmacokinetics--PK; *Hepatectomy; ***Liver** Function

Tests--methods--MT; Animals; Breath Tests; Carbon Dioxide--metabolism--ME; Carbon Isotopes; **Liver**--pathology--PA; **Liver**--surgery--SU; **Liver** Diseases--**diagnosis**--DI; **Liver** Diseases--pathology--PA; Organ Size; Rats; Rats, Wistar
CAS Registry No.: 0 (Carbon Isotopes); 124-38-9 (Carbon Dioxide); 56-41-7 (Alanine)
Record Date Created: 20020307
Record Date Completed: 20020404

22/9/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2005 Dialog. All rts. reserv.
15112257 PMID: 14673728
Patients with severe liver cirrhosis **followed up by L-[1-(13)C] phenylalanine** breath **test.**
Ishii Yukimoto; Suzuki Shigeru; Kohno Tomohisa; Aoki Masaru; Goto Iori; Kohno Tadashi; Ito Asuka; **Asai Satoshi**
Medical Research Center, Division of Genetic and Genomic Research, Nihon University School of Medicine, Tokyo, Japan.
Journal of gastroenterology (Japan) 2003, 38 (11) p1086-90, ISSN 0944-1174 Journal Code: 9430794
Publishing Model Print
Document type: Case Reports; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS
Compared to healthy subjects, patients with severe **liver cirrhosis** (LC) are reported to show lower values in the L-[1-(13)C] phenylalanine **breath** test (PBT). We performed this test several times during the clinical course in two patients with severe **liver cirrhosis** (LC). Patient 1 was a 67-year-old woman with non-B, non-C LC and **hepatocellular carcinoma** (HCC) in the lateral **hepatic** segment. Because the patient wanted to receive nonsurgical treatment for HCC, intraarterial administration of zinostatin stimalamer was performed. The patient was hospitalized four times before her death from **liver** failure on December 20, 2000. During her clinical course, PBT was performed four times. Values for both the rate of **hepatic** phenylalanine oxidation (%(13)C dose h(-1)) and %(13)C cumulative excretion gradually decreased during her clinical course. Patient 2 was a 57-year-old man with **hepatitis** C virus (HCV)-positive LC. He was hospitalized seven times between December 1998 and his death on May 24, 2001. During his clinical course, PBT was performed four times. Values for both %(13)C dose h(-1) and %(13)C cumulative excretion decreased during his clinical course. We confirmed that PBT was useful for following the course of LC.
Tags: Female; Male; Research Support, Non-U.S. Gov't
Descriptors: ***Live** r **Cirrhosis** -- **diagnosis** --DI; *Phenylalanine--**diagnostic** use--DU; Aged; Breath Tests; Carbon Isotopes; Fatal Outcome; Humans; **Liver** --metabolism--ME; Middle Aged; Phenylalanine--metabolism--ME ; Severity of Illness Index
CAS Registry No.: 0 (Carbon Isotopes); 63-91-2 (Phenylalanine)
Record Date Created: 20031215
Record Date Completed: 20040324

22/9/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2005 Dialog. All rts. reserv.
14889512 PMID: 12873431

L-[1-13C] phenylalanine breath **test reflects phenylalanine hydroxylase activity of the whole** liver .

Ishii Yukimoto; Suzuki Shigeru; Kohno Tomohisa; Aoki Masaru; Kohno Tadashi; Ito Asuka; Takayama Tadatoshi; **Asai Satoshi**

Medical Research Center, Division of Genetic and Genomic Research, Nihon University School of Medicine, Itabashi-ku, Tokyo, Japan. yishii@med.nihon-u.ac.jp

Journal of surgical research (United States) Jun 1 2003, 112 (1) p38-42, ISSN 0022-4804 Journal Code: 0376340

Publishing Model Print

Document type: Clinical Trial; Controlled Clinical Trial; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

OBJECT: The purpose of this study was to perform L-[1-13C] phenylalanine **breath** test (PBT), measure phenylalanine hydroxylase (PAH) activity in **liver** tissue biopsies from patients, analyze the relationship between PBT results and PAH activity, and determine the time point at which measurements best reflect PAH activity in **liver** tissue. METHODS: PBT was performed in 25 patients (10 with normal **liver** and 15 with **liver cirrhosis**). After administering 10 mg/kg L-[1-13C] phenylalanine, 300 ml of expired air was collected over 90 min at 15-min intervals. The rate of **hepatic** phenylalanine oxidation (%13C dose h(-1)) at each time point was calculated from the amount of 13CO(2) in the **breath** ; assuming a CO(2) production rate of 300 mmol m(-2) body surface area per hour. Subsequently, we examined the relationship between the results of PBT and PAH activity. RESULTS: PAH activity of the whole **liver** was significantly decreased in **hepatic cirrhosis** patients ($P < 0.05$). The results of PBT %13C dose h(-1) correlated with the PAH activity/ **liver** , with correlation coefficients at 30, 45, and 60 min of more than 0.7, and the maximum correlation was at 30 min ($r = 0.821$, $P < 0.0001$). %13C cumulative excretion correlated with the PAH activity/ **liver** with correlation coefficients of more than 0.7 after 45 min. The maximum correlation was at 90 min ($r = 0.770$, $P = 0.001$). CONCLUSION: PBT values reflect PAH activity in the whole **liver** and, in particular, the % dose h(-1) at 30 min after oral administration highly correlates with PAH activity, providing an important indicator for monitoring changes in whole **liver** PAH activity.

Tags: Female; Male

Descriptors: *Breath Tests--methods--MT; * **Liver** --enzymology--EN; * **Liver Cirrhosis** --enzymology--EN; *Phenylalanine--pharmacokinetics--PK; *Phenylalanine Hydroxylase--metabolism--ME; Adult; Aged; Carbon Isotopes--**diagnostic** use--DU; Humans; **Liver** --pathology--PA; **Liver Cirrhosis** --pathology--PA; Middle Aged; Organ Size

CAS Registry No.: 0 (Carbon Isotopes); 63-91-2 (Phenylalanine)

Enzyme No.: EC 1.14.16.1 (Phenylalanine Hydroxylase)

Record Date Created: 20030722

Record Date Completed: 20030814

22/9/18 (Item 18 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

0014602786 BIOSIS NO.: 200300559217

L-(1-13C) phenylaianine breath **test reflects histological changes in the** liver .

AUTHOR: **Ishii Yukimoto** (Reprint); Suzuki Shigeru; Kohno Tomohisa; Aoki

Masaru; Kohno Tadashi; Ito Asuka; Takayama Tadatoshi; **Asai Satoshi**
AUTHOR ADDRESS: Medical Research Center, Division of Genetic and Genomic Research, Nihon University School of Medicine, Oyaguchi-Kami Machi, Itabashi, Tokyo, 173-8610, Japan**Japan
AUTHOR E-MAIL ADDRESS: yishii@med.nihon-u.ac.jp
JOURNAL: Journal of Surgical Research 114 (2): p120-125 October 2003 2003
MEDIUM: print
ISSN: 0022-4804 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
ABSTRACT: Objective: Compared with healthy individuals, patients with chronic **liver** disease reportedly have lower L-(1-13C) phenylalanine **breath** test (PBT) values. However, there is no report detailing the relationship between the results of PBT and pathological data in **liver** disease patients. This study was designed to investigate the degree of histological changes in the **liver** that induce PBT changes and the time of measurement that reflects the histological change. Materials and methods: PBT was performed in 47 patients (10 with a normal **liver** , and 37 with chronic **hepatitis** C). After administering 10 mg/kg L-(1-13C) phenylalanine, 300 mL of expired air was collected over 90 min at 15-min intervals. The rate of **hepatic** phenylalanine oxidation (%13C dose h-1) at each time point was calculated from the amount of 13CO2 in the exhaled air, assuming a CO2 production rate of 300 mmol m-2 body surface area per hour. Subsequently, we examined the relationship between the results of PBT and MIETAVIR pathological scoring. Results: The highest correlation coefficients between the fibrosis score and %13C dose h-1 and between the fibrosis score and %13C cumulative excretion were obtained at 45 min ($r=-0.779$, $R2=0.607$; $P<0.0001$) and 75 min ($r=-0.768$, $R2=0.590$; $P<0.0001$), respectively. Conclusion: PBT is a useful adjunct for detecting histological changes in the **liver** . The %13C dose h-1 value at 45 min and the %13C cumulative excretion value at 75 min of PBT are useful for detecting **hepatic** histological change.
REGISTRY NUMBERS: 124-38-9: carbon dioxide
DESCRIPTORS:
MAJOR CONCEPTS: Gastroenterology--Human Medicine, Medical Sciences
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)--aged, female, male, patient
ORGANISMS: PARTS ETC: **liver** --digestive system, histology
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: chronic **hepatitis** --digestive system disease; chronic **liver** disease--digestive system disease
MESH TERMS: **Hepatitis** , Chronic (MeSH); **Liver** Diseases (MeSH)
CHEMICALS & BIOCHEMICALS: L-{1-carbon-13}phenylalanine-- **diagnostic** -drug, pharmacokinetics; carbon dioxide
METHODS & EQUIPMENT: L-{1-carbon-13}phenylalanine breath test--clinical techniques, **diagnostic** techniques; METAVIR pathological scoring--clinical techniques, **diagnostic** techniques
MISCELLANEOUS TERMS: **diagnostic** accuracy
CONCEPT CODES:
10060 Biochemistry studies - General
12504 Pathology - Diagnostic
14004 Digestive system - Physiology and biochemistry
14006 Digestive system - Pathology
22003 Pharmacology - Drug metabolism and metabolic stimulators

24500 Gerontology
BIOSYSTEMATIC CODES:
86215 Hominidae

22/9/19 (Item 19 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0015320660 BIOSIS NO.: 200510015160
Ornithine breath **test as a method to evaluate functional** liver **volume**
AUTHOR: Aoki Masaru (Reprint); **Ishii Yukimoto; Asai Satoshi; Ishikawa Koichi;** Takayama Tadatoshi
AUTHOR ADDRESS: Nihon Univ, Sch Med, Div 3, Dept Surg, 30 Oyaguchi Kami Machi, Tokyo 1730032, Japan**Japan
AUTHOR E-MAIL ADDRESS: yishii@med.nihon-u.ac.jp
JOURNAL: Journal of Surgical Research 124 (1): p9-13 MAR 05 2005
ISSN: 0022-4804
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
ABSTRACT: Background. The purpose of this study was to investigate whether the functional **liver** volume can be measured from changes in expiratory (CO2)-C-13 levels after intravenous administration of L-[1, 2-C-13] ornithine, using a rat model of hepatectomy.Materials and methods. Under pentobarbital anesthesia, 30%, 70%, or 90% hepatectomy was performed. In the control group, simple laparotomy was performed. Then, 20 mg/kg L-[1, 2-C-13] ornithine was administered to rats via the femoral vein. A **breath** test was conducted 20 min after laparotomy. We examined the correlation of the sum of (CO2)-C-13 output (S) or a single point of (CO2)-C-13 level (SP) with **liver** weight/body weight (LW/BW) (%) every 15 min.Results. In all of the groups, the ornithine **breath** test (OBT) graph reached a plateau level at about 6 min. The correlation coefficient between S-15 and LW/BW was highest 0.952 ($P < 0.0001$). The correlation coefficient between SP14 and LW/BW was highest, 0.944 ($P < 0.0001$). The severity of **hepatic** injury could be evaluated, with significant differences in S5-15 and SP5-15 in all comparisons between groups.Conclusion. In the **breath** test with intravenously administered L-[1, 2-C-13] ornithine, functional **liver** volume could be evaluated accurately in a short period. (c) 2005 Elsevier Inc. All rights reserved.
REGISTRY NUMBERS: 124-38-9: carbon dioxide; 76-74-4: pentobarbital
DESCRIPTORS:
MAJOR CONCEPTS: Pharmacology; Cardiovascular System--Transport and Circulation; Methods and Techniques; Digestive System--Ingestion and Assimilation
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: Wistar rat (Muridae)--male
ORGANISMS: PARTS ETC: **liver** --digestive system; femoral vein--circulatory system
COMMON TAXONOMIC TERMS: Animals; Chordates; Mammals; Nonhuman Vertebrates ; Nonhuman Mammals; Rodents; Vertebrate
CHEMICALS & BIOCHEMICALS: carbon dioxide; pentobarbital--general anesthetic-drug
METHODS & EQUIPMENT: laparotomy--clinical techniques; hepatectomy--therapeutic and prophylactic techniques, clinical techniques; ornithine breath test--clinical techniques, **diagnostic** techniques
MISCELLANEOUS TERMS: functional **liver** volume

CONCEPT CODES:
10060 Biochemistry studies - General
10062 Biochemistry studies - Nucleic acids, purines and pyrimidines
12512 Pathology - Therapy
14004 Digestive system - Physiology and biochemistry
14504 Cardiovascular system - Physiology and biochemistry
22002 Pharmacology - General
22024 Pharmacology - Neuropharmacology
BIOSYSTEMATIC CODES:
86375 Muridae